



passmedicine PART 2

HEMATOLOGY

2024





A 40-year-old woman attends the emergency department with sudden onset abdominal pain. She feels nauseated and has vomited 4 times in the past 2 hours. Her past medical history includes hypothyroidism and vitiligo.

On examination, she has a temperature of 38.2°C. She has a heart rate of 135bpm with a blood pressure of 116/66mmHg. There is guarding and tenderness on palpation of her right iliac fossa. Rovsing's sign is positive. It is noted that she has mild bruising and petechiae over her back and extremities and on further questioning, she tells you she has been suffering from frequent nosebleeds over the past 2 weeks.

She is reviewed by the general surgical team who want to prepare her for theatre.

Investigations:

Hb	127 g/L	Male: (135-180) Female: (115 - 160)
Platelets	28 * 10 ⁹ /L	(150 - 400)
WBC	15.2 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	136 mmol/L	(135 - 145)
K ⁺	4.1 mmol/L	(3.5 - 5.0)
Urea	5.6 mmol/L	(2.0 - 7.0)
Creatinine	87 µmol/L	(55 - 120)
Prothrombin time (PT)	11 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	26 secs	(25-35 secs)
Fibrinogen	2.1 g/L	(2 - 4)
D-Dimer	275 ng/mL	(< 400)
CRP	60 mg/L	(< 5)

What is the next step in this patient's management?

- ☐ Intravenous immunoglobulin ×
- ☐ Plasma exchange ×
- ☐ Platelet transfusion ×
- ☐ Prednisolone ×

☐ Romiplostim



Submit answer

Reference ranges 

Score: **0%**

1 -

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CRP	60 mg/L	(< 5)

What is the next step in this patient's management?

- Intravenous immunoglobulin

41%
- Plasma exchange

13%
- Platelet transfusion

22%
- Prednisolone

23%

Human immunoglobulin (IVIG) is an alternative to steroids in treating ITP, particularly if the platelets need to be raised quickly

Important for me **Less important**



This patient has immune thrombocytopenic purpura (ITP) the immune-mediated destruction of platelets. It is more common in older females and those with a history of autoimmune disease. It may present as easy-bruising, petechiae or epistaxis or may be an incidental finding on routine blood tests as seen here. The first-line treatment of choice is oral prednisolone. However, in patients who do not respond to or have contraindications to prednisolone use or those who require a rapid rise of platelets (for example, prior to having surgery) then intravenous immunoglobulin (IVIG) can be given. This patient requires a rapid rise of platelets due to her urgent surgery for likely appendicitis making IVIG the more appropriate choice in this scenario.

Plasma exchange is not a treatment for ITP. However, it is the treatment of choice for thrombocytopenic thrombotic purpura (TTP) a rare acquired disorder of coagulation that is associated with fever, acute kidney injury, central nervous system dysfunction (including confusion, seizures or coma), thrombocytopenia and microangiopathic haemolytic anaemia.

Platelet transfusion is a treatment of choice in ITP. However, it is typically reserved for cases of an acute haemorrhagic event or cerebral haemorrhage. As this patient is otherwise well with only evidence of minor bleeding, it would not be the first-line treatment of choice.

Romiplostim is a thrombopoietin receptor agonist which is a 3rd-line agent to treat ITP. It is considered in patients who have not responded to 1st and 2nd line treatment or have symptoms of chronic ITP persisting for beyond 12 months.



Discuss (10)

Improve

Next question >

Immune thrombocytopenia (ITP) in adults ★

Immune (or idiopathic) thrombocytopenic purpura (ITP) is an immune-mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb/IIIa or Ib-V-IX complex.

Children with ITP usually have an acute thrombocytopenia that may follow infection or vaccination. In contrast, adults tend to have a more chronic condition.

ITP in adults

Epidemiology

- more common in older females

Presentation

- may be detected incidentally following routine bloods
- symptomatic patients may present with
 - petechiae, purpura
 - bleeding (e.g. epistaxis)
 - catastrophic bleeding (e.g. intracranial) is not a common presentation

Investigations

- full blood count: isolated thrombocytopenia
- blood film
- a bone marrow examination is no longer used routinely
- antiplatelet antibody testing has poor sensitivity and doesn't affect clinical management so is not commonly done

Management

- first-line treatment for ITP is oral prednisolone
- pooled normal human immunoglobulin (IVIG) may also be used
 - it raises the platelet count quicker than steroids, therefore may be used if active bleeding or an urgent invasive procedure is required
- splenectomy is now less commonly used

Evan's syndrome

- ITP in association with autoimmune haemolytic anaemia (AIHA)



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123



Next question >

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A



$\frac{1}{2}$



T



Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

 14  7

[2003 ITP guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Bleeding Disorders \(ITP vs TTP vs HUS vs DIC\)](#)


Dirty USMLE - YouTube

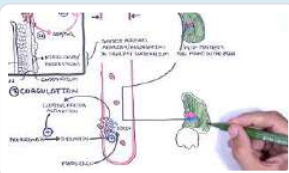
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[Immune thrombocytopenia \(ITP\)](#)



Osmosis - YouTube

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[Thrombocytopaenia \(low platelets\) Overview - platelet physiology, classification, pathophysiology](#)

Armando Hasudungan - YouTube

 2  1

[Report broken media](#)

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Question 2 of 191



A 50-year-old gentleman presents with fatigue and bruising to the emergency department. On examination, hepatosplenomegaly is noted, but no peripheral lymphadenopathy is palpable. The following blood tests are obtained:

Hb	73 g/l
Platelets	$43 \times 10^9/l$
WBC	$2.3 \times 10^9/l$
Neutrophils	$0.8 \times 10^9/l$
Lymphocytes	$1.3 \times 10^9/l$
Monocytes	$0.0 \times 10^9/l$
Basophils	$0.02 \times 10^9/l$
Eosinophils	$0.1 \times 10^9/l$

He is diagnosed with hairy cell leukaemia. Which gene is mutated in this malignant condition?

- ☐ BRCA1 ×
- ☐ BRAF ×
- ☐ TP53 ×
- ☐ NOTCH1 ×
- ☐ HER2 ×

Submit answer

Reference ranges 

Score: 0%

1 -



Question 2 of 191



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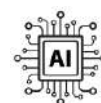
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Monocytes	$0.0 \times 10^9/l$
Basophils	$0.02 \times 10^9/l$
Eosinophils	$0.1 \times 10^9/l$

He is diagnosed with hairy cell leukaemia. Which gene is mutated in this malignant condition?

BRCA1	5%
BRAF	44%
TP53	24%
NOTCH1	22%
HER2	5%

BRAF is mutated in hairy cell leukaemia

Important for me Less important







Hairy cell leukaemia is caused by a mutation in exon 15 of the gene for the protein kinase BRAF. Patients may be asymptomatic with the disease is identified incidentally or present with symptoms of cytopenia.

The most common laboratory finding is cytopenia, usually affecting two or three lineages. Leucocyte counts tend to be low, with a monocytopenia present in 90% of patients. Hairy cells are often seen in peripheral blood films but their proportion is variable. They have a characteristic

appearance; lymphocytes with villous cytoplasmic projections, oval nuclei and finely mottled pale grey-blue cytoplasm.

A germline mutation in BRCA1 underlies an increased risk of malignancy (especially breast and ovarian) seen in some families. This gene is also mutated, as a somatic mutation, in other cases of breast and ovarian cancer. A germline mutation in TP53, encoding tumour suppressor protein p53, underlies Li Fraumeni syndrome. However, p53 is mutated in over 50% of malignancies, the most commonly mutated protein. Activating mutations in NOTCH1 are implicated in T cell acute lymphoblastic leukaemia and the HER2 gene is amplified in some forms of breast cancer. These are somatic mutations.

   Discuss (6)  Improve

Next question >

Hairy cell leukaemia ★

Hairy cell leukaemia is a rare malignant proliferation disorder of B cells. It is more common in males (4:1)

Features

- pancytopenia
- splenomegaly
- skin vasculitis in 1/3 patients
- 'dry tap' despite bone marrow hypercellularity
- tartrate resistant acid phosphatase (TRAP) stain positive

Management


- chemotherapy is first-line: cladribine, pentostatin
- immunotherapy is second-line: rituximab, interferon-alpha

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Next question >


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Textbooks

High-yield textbook

Extended textbook

Score: **12%**

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A 59-year-old woman presents to the haematology clinic for review. Despite treatment with cyclophosphamide, rituximab and fludarabine (FCR), she has experienced a steady rise in her lymphocyte count, accompanied by symptomatic anaemia. Examination reveals evidence of anaemia, her body mass index is 22 kg/m², and there is obvious splenomegaly.

Which of the following is the most appropriate intervention?

- | | | |
|-----------------------|------------|---|
| <input type="radio"/> | Ibrutinib | × |
| <input type="radio"/> | Lapatinib | × |
| <input type="radio"/> | Everolimus | × |
| <input type="radio"/> | Pazopanib | × |
| <input type="radio"/> | Sunitinib | × |

Submit answer

Reference ranges ▾

Score: 0%

1	-
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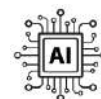
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Which of the following is the most appropriate intervention?

Ibrutinib	75%
Lapatinib	3%
Everolimus	8%
Pazopanib	2%
Sunitinib	12%

Ibrutinib is effective and can be used for the treatment of CLL in patients who have failed a previous therapy

Important for me Less important



Ibrutinib is a small molecule kinase inhibitor which binds to Bruton's tyrosine kinase which is involved in B cell clonal replication. It therefore has an important role in the treatment of B cell malignancies including mantle cell lymphoma and chronic lymphocytic leukaemia (CLL). It is recommended for patients who have had at least one previous therapy for CLL or those with a 17p deletion or TP53 mutation.

<https://www.nice.org.uk/guidance/ta429/chapter/1-Recommendations>

Lapatinib is a HER2 antagonist used in the treatment of HER2 positive breast cancer. Pazopanib and sunitinib are small molecule kinase inhibitors used in the treatment of renal carcinoma. Everolimus is an mTOR inhibitor used in the treatment of some solid tumours.



Discuss (7)
Improve

Next question >

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (> 10 cm) or progressive lymphadenopathy
- massive (> 6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever > 38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology



3



4

Media



Chronic Lymphocytic Leukemia (CLL) - Diagnosis & Treatment

Medicosis Perfectionalis - YouTube

👍 3 🗨️ 2



Chronic leukemia

Osmosis - YouTube

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Report broken media

Score: **12%**

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Question 4 of 191



A 76-year-old gentleman with myelofibrosis is found to have a haemoglobin of 67 g/l on admission. He is transfused two units of red cells and discharged home three days later. Six days later, he is readmitted febrile and jaundiced. Blood tests show:

Hb	71 g/l	Na ⁺	137 mmol/l	Bilirubin	39 µmol/l
Platelets	97 * 10 ⁹ /l	K ⁺	3.9 mmol/l	ALP	82 u/l
WBC	2.8 * 10 ⁹ /l	Urea	4.9 mmol/l	ALT	15 u/l
Neuts	1.5 * 10 ⁹ /l	Creatinine	79 µmol/l	Albumin	26 g/l

What is the most appropriate management for this condition?

- ☐ Prednisolone ×
- ☐ Intravenous immunoglobulin ×
- ☐ Conservative management ×
- ☐ Packed red cells ×
- ☐ Tazocin ×

Submit answer

Reference ranges 

Score: **0%**

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- 4** -



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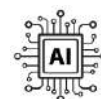
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Neuts	1.5 * 10 ⁹ /l	Creatinine	79 µmol/l	Albumin	26 g/l

What is the most appropriate management for this condition?

Prednisolone	30%
Intravenous immunoglobulin	21%
Conservative management	31%
Packed red cells	2%
Tazocin	16%

A delayed transfusion reaction occurs 7-10 days after the transfusion

Important for me Less important



This is a delayed transfusion reaction, which typically occurs 7-10 days post-transfusion. It occurs when patients are sensitised from previous transfusions or pregnancy and have alloantibodies against red cell antigens which are not picked up by cross-matching, if below detectable limits.

Management includes informing the laboratory and sending a repeat group and save sample for further testing. Usually, supportive management is sufficient, though if symptomatic from anaemia, they may require further transfusion after the further crossmatching testing is carried out. Prednisolone and intravenous immunoglobulin are not used in this situation typically. If this were bacterial contamination of the blood product, tazocin would be appropriate, though this presentation is too late and there are no other signs of sepsis.

[Discuss \(4\)](#)[Improve](#)[Next question >](#)

Blood product transfusion complications ★

Blood product transfusion complications may be broadly classified into the following:

- immunological: acute haemolytic, non-haemolytic febrile, allergic/anaphylaxis
- infective
- transfusion-related acute lung injury (TRALI)
- transfusion-associated circulatory overload (TACO)
- other: hyperkalaemia, iron overload, clotting

The table below summaries some of the key features:

Reaction	Features	Management
Non-haemolytic febrile reaction Thought to be caused by antibodies reacting with white cell fragments in the blood product and cytokines that have leaked from the blood cell during storage	Fever, chills Red cell transfusion (1-2%) Platelet transfusion (10-30%)	Slow or stop the transfusion Paracetamol Monitor
Minor allergic reaction Thought to be caused by foreign plasma proteins	Pruritus, urticaria	Temporarily stop the transfusion Antihistamine Monitor
Anaphylaxis Can be caused by patients with IgA deficiency who have anti-IgA antibodies	Hypotension, dyspnoea, wheezing, angioedema.	Stop the transfusion IM adrenaline ABC support <ul style="list-style-type: none">• oxygen• fluids
Acute haemolytic reaction ABO-incompatible blood e.g. secondary to human error	Fever, abdominal pain, hypotension	Stop transfusion Confirm diagnosis

Reaction	Features	Management
		<ul style="list-style-type: none"> check the identity of patient/name on blood product send blood for direct Coombs test, repeat typing and cross-matching <p>Supportive care</p> <ul style="list-style-type: none"> fluid resuscitation
<p>Transfusion-associated circulatory overload (TACO)</p> <p>Excessive rate of transfusion, pre-existing heart failure</p>	Pulmonary oedema, hypertension	<p>Slow or stop transfusion</p> <p>Consider intravenous loop diuretic (e.g. furosemide) and oxygen</p>
<p>Transfusion-related acute lung injury (TRALI)</p> <p>Non-cardiogenic pulmonary oedema thought to be secondary to increased vascular permeability caused by host neutrophils that become activated by substances in donated blood</p>	Hypoxia, pulmonary infiltrates on chest x-ray, fever, hypotension	<p>Stop the transfusion</p> <p>Oxygen and supportive care</p>

Further information is provided below:

Acute haemolytic transfusion reaction

Acute haemolytic transfusion reaction results from a mismatch of blood group (ABO) which causes massive intravascular haemolysis. This is usually the result of red blood cell destruction by IgM-type antibodies.

Symptoms begin minutes after the transfusion is started and include a fever, abdominal and chest pain, agitation and hypotension.

Treatment should include immediate transfusion termination, generous fluid resuscitation with saline solution and informing the lab

Complications include disseminated intravascular coagulation, and renal failure

Non-haemolytic febrile reaction

Febrile reactions

- due to white blood cell HLA antibodies
- often the result of sensitization by previous pregnancies or transfusions
- paracetamol may be given

Allergic/anaphylaxis reaction

Allergic reactions to blood transfusions are caused by hypersensitivity reactions to components within the transfusion. Symptoms typically arise within minutes of starting the transfusion and severity can range from urticaria to anaphylaxis with hypotension, dyspnoea, wheezing, and stridor, or angioedema.

Simple urticaria should be treated by discontinuing the transfusion and with an antihistamine. Once the symptoms resolve, the transfusion may be continued with no need for further workup.

More severe allergic reaction or anaphylaxis should be treated urgently. The transfusion should be permanently discontinued, intramuscular adrenaline should be administered and supportive care. Antihistamine, corticosteroids and bronchodilators should also be considered for these patients.

Transfusion-related acute lung injury (TRALI)

A rare but potentially fatal complication of blood transfusion. Characterised by the development of hypoxaemia / acute respiratory distress syndrome within 6 hours of transfusion. Features include:

- hypoxia
- pulmonary infiltrates on chest x-ray
- fever
- hypotension

Transfusion-associated circulatory overload (TACO)

A relatively common reaction due to fluid overload resulting in pulmonary oedema. As well as features of pulmonary oedema the patient may also be hypertensive, a key difference from patients with TRALI.

Infective

Bacterial and viral

The risk of infectious complications varies with different types of blood products due to their storage conditions, components involved, and duration of storage.

Red Blood Cells (RBCs)

- Pathogens: RBCs are primarily at risk for transmitting viral agents such as HIV, HBV, and HCV. Bacterial contamination is less common but possible, particularly from skin flora during collection.
- Clinical impact: Viral infections can lead to chronic disease states such as chronic hepatitis or AIDS. Bacterial infections may manifest as sepsis if not promptly treated.

Platelets

- Pathogens: Platelets are stored at room temperature, which increases the risk of bacterial proliferation. Common contaminants include *Staphylococcus epidermidis* and *Bacillus cereus*.
- Clinical impact: Bacterial contamination of platelets is more likely to lead to rapid onset of sepsis and septic shock, given the optimal growth conditions during storage.

Prions

Transmission of vCJD

- although the absolute risk is very small, vCJD may be transmitted via blood transfusion
- a number of steps have been taken to minimise this risk, including:
 - from late 1999 onward, all donations have undergone removal of white cells (leucodepletion) in order to reduce any vCJD infectivity present
 - from 1999, plasma derivatives have been fractionated from imported plasma rather than being sourced from UK donors. Fresh Frozen Plasma (FFP) used for children and certain groups of adults needing frequent transfusions is also imported
 - from 2004 onward, recipients of blood components have been excluded from donating blood



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Links

Serious Hazards of Transfusion

 6  16

[SHOT website](#)

Gov.uk

 6  11

[2013 vCJD and Transfusion of Blood Components: an Updated Risk Assessment](#)

British Journal of Haematology

 11  14

[Algorithm for managing an acute transfusion reaction](#)

[Suggest link](#)

[Report broken link](#)

Media




[Blood transfusion reactions and transplant rejection](#)


Osmosis - YouTube


 3  1


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Score: **12%**

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A 44-year-old woman is referred to ambulatory care with a 10-day history of lethargy and exertional dyspnoea. Prior to this episode, she reports having mild coryzal symptoms that have since settled. Her past medical history is only significant for hypothyroidism which is well-controlled on levothyroxine.

A full screen of blood tests is sent:

Hb	71 g/L	(135 - 180)
Platelets	$110 \times 10^9/L$	(150 - 400)
WBC	$7.0 \times 10^9/L$	(4.0 - 11.0)
Urea	6.3 mmol/L	(2.0 - 7.0)
Creatinine	110 $\mu\text{mol/L}$	(55 - 120)

Prothrombin time (PT)	11 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	26 secs	(25-35 secs)
Fibrinogen	3.1 g/L	(2 - 4)
D-Dimer	345 ng/mL	(< 400)
Reticulocytes	2.5 %	(0.5 - 1.5)
Blood film	Schistocytes	
Coombs test	Negative	

Bilirubin	59 $\mu\text{mol/L}$	(3 - 17)
ALP	128 u/L	(30 - 100)
ALT	40 u/L	(0 - 40)
AST	50 u/L	(< 35)
Blood glucose	5.2 mmol/L	(4 - 7)
Total cholesterol	7.1 mmol/L	(< 5)

What is the most likely diagnosis?

☐ Autoimmune haemolytic anaemia



☐ Disseminated intravascular coagulation



<input type="radio"/>	Paroxysmal nocturnal haemoglobinuria	×
<input type="radio"/>	Thrombotic thrombocytopenia purpura	×
<input type="radio"/>	Zieve syndrome	×

Submit answer

Reference ranges ▾

Score: 0%	
1	-
2	-
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A 44-year-old woman is referred to ambulatory care with a 10-day history of lethargy and exertional dyspnoea. Prior to this episode, she reports having mild coryzal symptoms that have since settled. Her past medical history is only significant for hypothyroidism which is well-controlled on levothyroxine.

A full screen of blood tests is sent:

Hb	71 g/L	(135 - 180)
Platelets	110 * 10 ⁹ /L	(150 - 400)
WBC	7.0 * 10 ⁹ /L	(4.0 - 11.0)
Urea	6.3 mmol/L	(2.0 - 7.0)
Creatinine	110 µmol/L	(55 - 120)

Prothrombin time (PT)	11 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	26 secs	(25-35 secs)
Fibrinogen	3.1 g/L	(2 - 4)
D-Dimer	345 ng/mL	(< 400)
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Coombs test	Negative	

Bilirubin	59 µmol/L	(3 - 17)
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ALT	40 u/L	(0 - 40)
AST	50 u/L	(< 35)
Blood glucose	5.2 mmol/L	(4 - 7)
Total cholesterol	7.1 mmol/L	(< 5)

What is the most likely diagnosis?

Autoimmune haemolytic anaemia

22%

Disseminated intravascular coagulation

2%

Paroxysmal nocturnal haemoglobinuria

13%

Thrombotic thrombocytopenia purpura

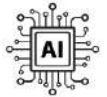
10%

Zieve syndrome

53%

Zieve syndrome is a rare clinical syndrome of Coombs-negative haemolysis, cholestatic jaundice, and transient hyperlipidaemia

Important for me Less important



This patient has a likely diagnosis of **Zieve syndrome** given the triad of non-autoimmune haemolysis, jaundice and hyperlipidaemia. The negative Coombs test indicates non-autoimmune haemolytic anaemia. In Zieve syndrome, jaundice can be cholestatic in nature but also secondary to haemolysis. The raised ALP supports a cholestatic picture. Zieve syndrome is a rare syndrome and generally resolves following the cessation of alcohol use.

Autoimmune haemolytic anaemia is incorrect. Although there is evidence of haemolysis given the low Hb, reticulocytosis, raised bilirubin and presence of schistocytes, the Coombs test is negative. A negative Coombs test makes autoimmune haemolytic anaemia very unlikely.

Disseminated intravascular coagulation (DIC) is incorrect. DIC is a disease of abnormal coagulopathy characterised by a prolonged prothrombin time, prolonged APTT, low fibrinogen and a very high D-dimer. Triggers for DIC include malignancy, surgery and significant infection of which none are mentioned in this presentation. The resolved coryzal symptoms are unlikely to be significant.

Paroxysmal nocturnal haemoglobinuria (PNH) is incorrect. PNH is characterised by intravascular haemolysis, bone marrow hypoplasia and increased risk of thromboses. This does not completely fit the patient's presentation making this answer incorrect.

Thrombotic thrombocytopenia purpura (TTP) is incorrect. This condition presents as a pentad of fever, acute kidney injury, thrombocytopenia, microangiopathic haemolytic anaemia and cerebral dysfunction. The absence of the majority of these features makes TTP unlikely.



Discuss (3)

Improve

Next question >

Haemolytic anaemias: by cause ★

Hereditary haemolytic anaemias can be subdivided into membrane, metabolism or haemoglobin defects

Hereditary causes

- membrane: hereditary spherocytosis/elliptocytosis
- metabolism: G6PD deficiency
- haemoglobinopathies: sickle cell, thalassaemia

Acquired haemolytic anaemias can be subdivided into immune and non-immune causes

Acquired: immune causes (Coombs-positive)

- autoimmune: warm/cold antibody type
- alloimmune: transfusion reaction, haemolytic disease newborn
- drug: methyldopa, penicillin

Acquired: non-immune causes (Coombs-negative)

- microangiopathic haemolytic anaemia (MAHA): TTP/HUS, DIC, malignancy, pre-eclampsia
- prosthetic heart valves
- paroxysmal nocturnal haemoglobinuria
- infections: malaria
- drug: dapsone
- Zieve syndrome
 - rare clinical syndrome of Coombs-negative haemolysis, cholestatic jaundice, and transient hyperlipidaemia associated with heavy alcohol use, typically following a binge
 - typically resolves with abstinence from alcohol



123



Next question >

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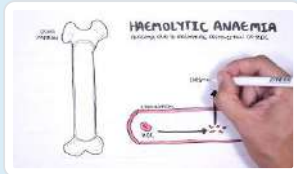


Textbooks

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Extended textbook

Media



Haemolytic Anaemia - classification (intravascular, extravascular), pathophysiology, investigations

Armando Hasudungan - YouTube

👍 3 👎 2

[Report broken media](#)

Score: **12%**

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- 50 ✖



A 54-year-old gentleman is admitted under the medical team with a diagnosis of urosepsis. Twenty four hours after admission he develops numerous bruises across his abdomen, arms and legs. It is also noted that he is bleeding from his cannula site

His blood results are as follows

Hb	110 x10 ¹² /L	130-168 x10 ¹² /L
WCC	19 x10 ⁹ /L	4.2-10.6 x10 ⁹ /L
Platelets	50 x10 ⁹ /L	130-370 x10 ⁹ /L
CRP	300 mg/L	0-5 mg/L
Fibrinogen	3.8 g/L	1.8-4.0 g/L
PT	20s	9-12s
APTT	38s	23-31s
Creatinine	150µmol/L	60-125 µmol/L
eGFR	60 mL/min/1.73 m ²	>90 mL/min/1.73 m ²

What is the most likely cause?

- ☐ Idiopathic thrombocytopenia purpura (ITP) ×
- ☐ Thrombotic thrombocytopenia purpura (TTP) ×
- ☐ Disseminated intravascular coagulation (DIC) ×
- ☐ Heparin induced thrombocytopenia (HIT) ×
- ☐ Haemolytic uraemia syndrome (HUS) ×

Submit answer

Reference ranges 

Score: **0%**

- 1 -
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- 6 -**

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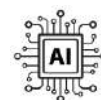
Hb	110 x10 ¹² /L	130-168 x10 ¹² /L
WCC	19 x10 ⁹ /L	4.2-10.6 x10 ⁹ /L
Platelets	50 x10 ⁹ /L	130-370 x10 ⁹ /L
CRP	300 mg/L	0-5 mg/L
Fibrinogen	3.8 g/L	1.8-4.0 g/L
PT	20s	9-12s
APTT	38s	23-31s
Creatinine	150µmol/L	60-125 µmol/L
eGFR	60 mL/min/1.73 m ²	>90 mL/min/1.73 m ²

What is the most likely cause?

Idiopathic thrombocytopenia purpura (ITP)	7%
Thrombotic thrombocytopenia purpura (TTP)	11%
Disseminated intravascular coagulation (DIC)	61%
Heparin induced thrombocytopenia (HIT)	6%
Haemolytic uraemia syndrome (HUS)	15%

In DIC fibrinogen can be normal or elevated in over 50% of cases especially early on (as fibrinogen is an acute phase marker)

Important for me Less important




Fibrinogen is an acute phase marker. Therefore in DIC fibrinogen levels can be normal or elevated in over 50% of cases especially early on.

PT/APTT are usually normal in ITP, TTP, HUS and HIT

Renal function is markedly abnormal in HUS

In HIT the plasma prothrombin time (PT) is decreased but the activated partial thromboplastin time (aPTT), and the fibrinogen levels are normal.

		 Discuss (13)	Improve
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Next question >

Disseminated intravascular coagulation ★

Under homeostatic conditions, coagulation and fibrinolysis are coupled. The activation of the coagulation cascade yields thrombin that converts fibrinogen to fibrin; the stable fibrin clot being the final product of hemostasis. The fibrinolytic system breaks down fibrinogen and fibrin. Activation of the fibrinolytic system generates plasmin (in the presence of thrombin), which is responsible for the lysis of fibrin clots. The breakdown of fibrinogen and fibrin results in polypeptides (fibrin degradation products). In a state of homeostasis, the presence of plasmin is critical, as it is the central proteolytic enzyme of coagulation and is also necessary for fibrinolysis.

In DIC, the processes of coagulation and fibrinolysis are dysregulated, and the result is widespread clotting with resultant bleeding. Regardless of the triggering event of DIC, once initiated, the pathophysiology of DIC is similar in all conditions. One critical mediator of DIC is the release of a transmembrane glycoprotein (tissue factor = TF). TF is present on the surface of many cell types (including endothelial cells, macrophages, and monocytes) and is not normally in contact with the general circulation, but is exposed to the circulation after vascular damage. For example, TF is released in response to exposure to cytokines (particularly interleukin 1), tumour necrosis factor, and endotoxin. This plays a major role in the development of DIC in septic conditions. TF is also abundant in tissues of the lungs, brain, and placenta. This helps to explain why DIC readily develops in patients with extensive trauma. Upon activation, TF binds with coagulation factors that then triggers the extrinsic pathway (via Factor VII) which subsequently triggers the intrinsic pathway (XII to XI to IX) of coagulation.

Causes of DIC

- sepsis
- trauma
- obstetric complications e.g. amniotic fluid embolism or hemolysis, elevated liver function tests, and low platelets (HELLP syndrome)
- malignancy

Diagnosis

A typical blood picture includes:

- ↓ platelets
- ↓ fibrinogen
- ↑ PT & APTT
- ↑ fibrinogen degradation products
- schistocytes due to microangiopathic haemolytic anaemia


Disorder	Prothrombin time	APTT	Bleeding time	Platelet count
Warfarin administration	Prolonged	Normal	Normal	Normal
Aspirin administration	Normal	Normal	Prolonged	Normal
Heparin	Often normal (may be prolonged)	Prolonged	Normal	Normal
DIC	Prolonged	Prolonged	Prolonged	Low

 + Q 123 


Next question >


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Textbooks

High-yield textbook

Extended textbook

Media



Disseminated intravascular coagulation

Osmosis - YouTube



2



1

[Report broken media](#)

Score: **12%**

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You are called to see a 68-year-old female on the oncology ward who has developed coffee ground vomiting. She has a diagnosis of colorectal cancer which she is currently undergoing curative chemotherapy for.

Blood results are as follows:

Hb	95 g/l
Platelets	34 * 10 ⁹ /l
WBC	14 * 10 ⁹ /l
PT ratio	2.4
aPPT ratio	2.1
D-dimer	1540 ng/ml (normal < 500)
Fibrinogen	0.8 g/l (normal 1.5-4.0)

You administer fresh frozen plasma. Repeat blood results are as follows:

Hb	91 g/l
Platelets	24 * 10 ⁹ /l
WBC	18.4 * 10 ⁹ /l
PT ratio	2.2
aPPT ratio	1.9
Fibrinogen	0.85 g/l (normal 1.5-4.0)

What treatment is indicated?

- ☐ Cryoprecipitate ×
- ☐ Vitamin K ×
- ☐ Factor VIII ×
- ☐ Factor IX ×
- ☐ No further treatment ×

Submit answer

Reference ranges ▾

Score: 0%	
1	-
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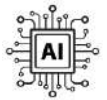
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WBC	18.4 * 10 ⁹ /l
PT ratio	2.2
aPPT ratio	1.9
Fibrinogen	0.85 g/l (normal 1.5-4.0)

What treatment is indicated?

Cryoprecipitate	81%
Vitamin K	7%
Factor VIII	4%
Factor IX	0%
No further treatment	7%

In bleeding patients with DIC with severe hypofibrinogenaemia (<1 g/l) that persists despite FFP replacement, then fibrinogen concentrate or cryoprecipitate is indicated

Important for me Less important



The patient has DIC likely secondary to malignancy. In bleeding patients with DIC and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), administration of fresh frozen plasma (FFP) may be useful. Notably, this patient continues to have severe hypofibrinogenaemia despite administration of FFP. In bleeding patients with DIC with severe hypofibrinogenaemia (<1 g/l) that persists despite FFP replacement, then fibrinogen concentrate or cryoprecipitate is indicated.

Vitamin K would be indicated in Vitamin K deficiency. There is nothing in the history to suggest vitamin K deficiency.

Factor VIII and factor IX are indicated for Haemophilia A and B respectively.

		Discuss (4)	Improve
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Next question >

Disseminated intravascular coagulation ★

Under homeostatic conditions, coagulation and fibrinolysis are coupled. The activation of the coagulation cascade yields thrombin that converts fibrinogen to fibrin; the stable fibrin clot being the final product of hemostasis. The fibrinolytic system breaks down fibrinogen and fibrin. Activation of the fibrinolytic system generates plasmin (in the presence of thrombin), which is responsible for the lysis of fibrin clots. The breakdown of fibrinogen and fibrin results in polypeptides (fibrin degradation products). In a state of homeostasis, the presence of plasmin is critical, as it is the central proteolytic enzyme of coagulation and is also necessary for fibrinolysis.

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DIC	Prolonged	Prolonged	Prolonged	Low



123



Next question >

B

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Textbooks

High-yield textbook

Extended textbook

Media



Disseminated intravascular coagulation

Osmosis - YouTube



2



1

[Report broken media](#)

Score: **12%**

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A 74-year-old woman is referred to the medical assessment unit with diffuse bone pain affecting her back and ribs that has persisted for two months. She has no significant past medical history and is not on any regular medications. She does not smoke and still works as a potter.

Clinical examination is unremarkable and there are no focal areas of tenderness or swelling. There is no organomegaly or lymphadenopathy. Cardio-respiratory examination is unremarkable.

Blood tests:

Hb	111 g/L	Male: (135-180) Female: (115 - 160)
Platelets	389 * 10 ⁹ /L	(150 - 400)
WBC	4.2 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	4.8 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	10 mg/L	(< 5)
Calcium	2.68 mmol/L	(2.20-2.60)
Immunoglobulin G	24.1 g/L	(6.6 - 15.9)
Immunoglobulin A	4.4 g/L	(0.6-5)
Immunoglobulin M	2.2 g/L	(0.53 - 2.47)

Serum protein electrophoresis:

Paraprotein	present
-------------	---------

Given the likely diagnosis, what is the first-line imaging investigation?

- ☐ Isotope bone scan ×
- ☐ Low dose whole body CT ×
- ☐ Fluorodeoxyglucose positron emission tomography CT (FDG PET-CT) ×
- ☐ Plain radiographic skeletal survey ×

☐ Whole body MRI



Submit answer

Reference ranges 

Score: **0%**

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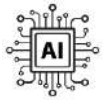
Serum protein electrophoresis:

Paraprotein	present
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Given the likely diagnosis, what is the first-line imaging investigation?

Isotope bone scan	4%
Low dose whole body CT	3%
Fluorodeoxyglucose positron emission tomography CT (FDG PET-CT)	7%
Plain radiographic skeletal survey	15%

Whole body MRI 1st line imaging in suspected multiple myeloma

Important for me Less important

Whole-body MRI is the correct answer. This patient presents with diffuse bone pain, anaemia, hypercalcaemia, raised IgG and a paraprotein. She likely has multiple myeloma. Recent NICE guidelines state that imaging should be offered to all patients with suspected myeloma and that whole-body MRI is the first-line choice in the absence of contraindication.

Low dose whole-body CT is incorrect. This investigation can be offered if an MRI is contraindicated or not tolerated.

A plain radiographic skeletal survey is incorrect. This is only offered if CT or MRI are unsuitable or not tolerated.

Isotope bone scan is incorrect. This is not recommended in the investigation of suspected myeloma.

FDG PET-CT is incorrect. This imaging investigation is only an option for those patients with confirmed multiple myeloma who have not yet had any whole body imaging.



Discuss (1)

Improve

Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia

- primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
- much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
- this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



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123



Next question >

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Links

Clinical Knowledge Summaries

 10  10

[Haematological cancers - recognition and referral](#)

NICE

 12  6

[2016 myeloma guidelines](#)

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Media



[Multiple Myeloma - Diagnosis and Treatment](#)



Medicosis Perfectionalis - YouTube

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[Multiple Myeloma](#)

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[Multiple Myeloma Mnemonic...the story of the plasma cell](#)

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What is multiple myeloma?

Khan Academy - YouTube

👍 4 🗨️ 1



Multiple Myeloma

Townsend Teaching - YouTube

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Multiple Myeloma

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Multiple Myeloma

Armando Hasudungan - YouTube

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Question 9 of 191



A 67-year-old man with a previous diagnosis of myelodysplasia presents to a haematology clinic with rapid weight loss, an increase in nosebleeds and a greater feeling of fatigue than previously. He has the single lineage dysplasia subtype and usually requires monthly transfusions, he has presented two weeks after his last red blood cell top-up.

His blood results are as follows:

Hb	66 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$9 \times 10^9/\text{L}$	(150 - 400)
WBC	$1.1 \times 10^9/\text{L}$	(4.0 - 11.0)

A blood film is sent for and he is admitted for blood and platelet transfusions.

What is the blood film likely to show?

☐ Burr cells
 ×

☐ Fragmented red blood cells
 ×

☐ Lymphoblasts
 ×

☐ Myeloblasts
 ×

☐ Smear cells
 ×

Submit answer

Reference ranges 

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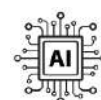
A blood film is sent for and he is admitted for blood and platelet transfusions.

What is the blood film likely to show?

Burr cells	15%
Fragmented red blood cells	14%
Lymphoblasts	3%
Myeloblasts	52%
Smear cells	15%

Myelodysplasia may progress to acute myeloid leukaemia

Important for me Less important



Myeloblasts is the correct answer as this is most likely a malignant transformation of myelodysplasia to acute myeloid leukaemia (AML). This is evidenced by the myeloblasts coupled with the significant drop in haemoglobin, platelets and white blood cells, with the B symptoms of weight loss and fatigue becoming more prominent. The clue in the blood tests is that he previously had single lineage dysplasia which causes refractory anaemia, but now he has platelet and white blood cell reduction indicating bone marrow failure. The white cells overproduced in AML are the immature myeloblasts, not normally found in the blood.

Burr cells are incorrect as these are spiculated red blood cells commonly found in chronic renal failure due to high levels of nitrogen in the blood destabilising the red cell membrane.

Lymphoblasts are incorrect as these cells are only found in the peripheral blood film in acute lymphoblastic leukaemia.

Smear cells are incorrect because they are the result of artefactual damage to mature lymphocytes during film production, often characteristic of chronic lymphoblastic leukaemia.

Fragmented red blood cells are seen in many conditions which result in intravascular haemolysis, such as renal failure, microangiopathic haemolytic anaemia, haemolytic uraemic syndrome or thrombotic thrombocytopenic purpura. The reason for the anaemia, in this case, is bone marrow failure as opposed to haemolysis.



Next question >

Myelodysplastic syndrome ★

Myelodysplastic syndromes (MDS) encompass a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, peripheral blood cytopenias, and a risk of progression to acute myeloid leukaemia (AML). These disorders predominantly affect older adults, with a median age at diagnosis of 70-75 years.

Aetiology and Pathophysiology

MDS arises from genetic mutations in hematopoietic stem cells.

Around 90% of cases are primary with the remaining 10% secondary to causes such as chemotherapy and radiotherapy. Secondary MDS typically develops around 5 years post-treatment.

The key pathophysiological feature of MDS is ineffective hematopoiesis leading to peripheral cytopenias despite a typically hypercellular bone marrow. The exact mechanisms are still not entirely understood, but they likely involve a combination of increased apoptosis, abnormal differentiation, and immune dysregulation.

Clinical Features

MDS can present with various symptoms related to the underlying cytopenias. Common presentations include fatigue, weakness, and pallor due to anaemia; recurrent infections due to neutropenia; and easy bruising or bleeding due to thrombocytopenia. Some patients may be asymptomatic and are diagnosed incidentally on routine blood counts.

Diagnosis

The diagnosis of MDS is based on peripheral blood counts, bone marrow examination, and cytogenetic analysis. Bone marrow biopsy typically shows dysplastic changes in hematopoietic cells and a varying degree of blasts. Cytogenetic analysis can identify specific chromosomal abnormalities that may have prognostic implications.

Treatment

Treatment of MDS depends on the subtype of MDS, the patient's age and overall health, and the severity of symptoms. Options include supportive care (e.g., blood transfusions, growth factors), disease-modifying therapy (e.g., hypomethylating agents, lenalidomide), immunosuppressive therapy, and hematopoietic stem cell transplantation. The latter is the only potentially curative option but is limited by the patient's age and comorbidities.



123



Next question >

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[Myelodysplastic syndromes](#)

Osmosis - YouTube



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An 18-year-old woman presents to the haematology clinic with spontaneous bruising, heavy periods and recurrent epistaxis. This has been a continuous problem during her teenage years but she was recently found to have anaemia and received an iron transfusion which prompted further investigation into these symptoms.

On examination, she is well and alert. There are numerous purpura across both arms and she denies trauma or any itchiness.

Hb	98 g/l
Platelets	$314 \times 10^9/l$
WBC	$5.6 \times 10^9/l$
PT	13.8
APTT	34.3
PFA-100 assay	prolonged closure time
Flow cytometry	GPIIb/IIIa negative
Ristocetin-induced platelet aggregation	normal agglutination

What is the likely diagnosis?

- ☐ Bernard-Soulier disease ×
- ☐ Glanzmann thrombasthenia ×
- ☐ Von Willebrand disease ×
- ☐ Haemophilia A ×
- ☐ Evan's syndrome ×

Submit answer

Reference ranges 

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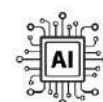
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PFA-100 assay	prolonged closure time
Flow cytometry	GPIIb/IIIa negative
Ristocetin-induced platelet aggregation	normal agglutination

What is the likely diagnosis?

Bernard-Soulier disease	16%
Glanzmann thrombasthenia	31%
Von Willebrand disease	35%
Haemophilia A	9%
Evan's syndrome	9%

Innate defective glycoprotein IIb/IIIa -> Glanzmann's thrombasthenia

Important for me Less important



This is a test of the coagulopathies. Von Willebrand disease and haemophilia tend to have raised APTT. Evan's syndrome is an autoimmune disease with low platelets and red blood cells. The PFA-100 assay shows that platelets are not aggregating and this may be due to platelet glycoproteins

or their interaction with von willebrand factor. The ristocetin effectively allows aggregation of von willebrand factor to GPIb and does not require GPIIb/IIIa. Therefore Glanzmann thrombasthenia will have normal platelet aggregation once ristocetin is added.

Discuss (16)

Improve

Next question >

Glanzmann's thrombasthenia ★

Glanzmann's thrombasthenia is rare autosomal recessive platelet disorder caused by qualitative or quantitative deficiencies in GpIIb/IIIa, the receptor for fibrinogen.

Note the contrast to ITP, where antibodies are formed against GpIIb/IIIa.

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Next question >

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A 48-year-old man was admitted to the acute medical unit with history of haematemesis and melaena. No previous history was available. He required fluid resuscitation and had eight-units of red cell transfusion. On review after his transfusion, his pulse was found to be 80 beats per minute and blood pressure 130/78mmHg. Chest and abdominal examination were essentially normal. Repeat bloods were taken and results are as shown below:

Hb	110g/l (130 - 180)
Platelets	$80 \times 10^9/l$ (150 - 400)
WBC	$10 \times 10^9/l$ (4.0 - 11.0)
Prothrombin time	14.2secs (11.5 - 15.5)
INR	1.3 (<1.4)
APTT	32secs (30 - 40)
Thrombin time	17secs (15 - 19)
Fibrinogen	2.1g/l (1.8 - 5.4)

Which blood product should he be given at this stage?

- ☐ Cryoprecipitate and fresh frozen plasma ×
- ☐ Fresh-frozen plasma ×
- ☐ Fresh-frozen plasma and platelets ×
- ☐ Platelets ×
- ☐ No blood products are indicated ×

Submit answer

Reference ranges 

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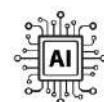
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INR	1.3 (<1.4)
APTT	32secs (30 - 40)
Thrombin time	17secs (15 - 19)
Fibrinogen	2.1g/l (1.8 - 5.4)

Which blood product should he be given at this stage?

Cryoprecipitate and fresh frozen plasma	5%
Fresh-frozen plasma	9%
Fresh-frozen plasma and platelets	6%
Platelets	6%
No blood products are indicated	74%

Fresh frozen plasma is offered to bleeding patients who have either a prothrombin time or activated partial thromboplastin time greater than 1.5 times normal

Important for me Less important



Decisions on transfusion of blood products should recognize that over-transfusion may be as damaging as under-transfusion by exposing patients to the risk of fluid overload and other complications of transfusion. Do not offer platelet transfusion to patients who are not actively bleeding and are haemodynamically stable. Platelets may be given to those actively bleeding and

have a platelet count of less than $50 \times 10^9/L$. Offer fresh frozen plasma to bleeding patients who have either a prothrombin time or activated partial thromboplastin time greater than 1.5 times normal; and cryoprecipitate or fibrinogen concentrate to those with a fibrinogen level of less than 1 g/L. Offer prothrombin complex concentrate to patients who are taking warfarin and actively bleeding. Treat patients who are taking warfarin and whose upper gastrointestinal bleeding has stopped in line with local warfarin protocols.



Discuss (6)

Improve

Next question >

Blood products: FFP, cryoprecipitate and prothrombin complex ★

NICE published guidelines on the use of blood products in 2015.

Fresh frozen plasma (FFP)

- most suited for 'clinically significant' but without 'major haemorrhage' in patients with a prothrombin time (PT) ratio or activated partial thromboplastin time (APTT) ratio > 1.5
- typically 150-220 mL
- can be used prophylactically in patients undergoing invasive surgery where there is a risk of significant bleeding
- In contrast to red cells, the universal donor of FFP is AB blood because it lacks any anti-A or anti-B antibodies

Cryoprecipitate

- contains concentrated Factor VIII:C, von Willebrand factor, fibrinogen, Factor XIII and fibronectin, produced by further processing of Fresh Frozen Plasma (FFP). Clinically it is most commonly used to replace fibrinogen
- much smaller volume than FFP, typically 15-20mL
- most suited for patients for 'clinically significant' but without 'major haemorrhage' who have a fibrinogen concentration < 1.5 g/L
- example use cases include disseminated intravascular coagulation, liver failure and hypofibrinogenaemia secondary to massive transfusion. It may also be used in an emergency situation for haemophiliacs (when specific factors not available) and in von Willebrand disease
- can be used prophylactically in patients undergoing invasive surgery where there is a risk of significant bleeding where the fibrinogen concentration < 1.0 g/L

Prothrombin complex concentrate

- used for the emergency reversal of anticoagulation in patients with either severe bleeding or a head injury with suspected intracerebral haemorrhage
- can be used prophylactically in patients undergoing emergency surgery depending on the particular circumstance



123

[Next question >](#)**B***I***A****T**

Textbooks

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Links

NICE



6



6

[2015 Blood transfusion guidelines](#)[Suggest link](#)[Report broken link](#)Score: **12%**

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A 65-year-old man has been admitted with worsening abdominal pain, hypotension and altered mental state. He is currently being treated for intra-abdominal sepsis secondary to peritoneal dialysis for chronic renal failure secondary to diabetic nephropathy. Previous medical history includes type 2 diabetes mellitus, angina, hypertension, hyperlipidaemia, and diabetic retinopathy. The patient is not anti-coagulated but does take aspirin.

He is started on intravenous antibiotics and intravenous fluid.

His results are:

Hb	91 g/L	Male: (135-180) Female: (115 - 160)
Platelets	60 * 10 ⁹ /L	(150 - 400)
WBC	24.5 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	128 mmol/L	(135 - 145)
K ⁺	5.8 mmol/L	(3.5 - 5.0)
Urea	31.7 mmol/L	(2.0 - 7.0)
Creatinine	645 µmol/L	(55 - 120)
CRP	317 mg/L	(< 5)
PT	22 seconds	(10-14 seconds)
APTT	56 seconds	(30-40 seconds)

He undergoes a CT scan which shows a spontaneous retroperitoneal haemorrhage and is referred to interventional radiology.

Given the patient's coagulation profile, what blood product is needed?

- ☐ Cryoprecipitate ×
- ☐ Fresh frozen plasma ×
- ☐ Protamine ×
- ☐ Prothrombin complex concentrates ×
- ☐ Recombinant activated factor 7 ×

Submit answer

Reference ranges ▾

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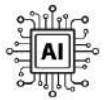
He undergoes a CT scan which shows a spontaneous retroperitoneal haemorrhage and is referred to interventional radiology.

Given the patient's coagulation profile, what blood product is needed?

Cryoprecipitate	12%
Fresh frozen plasma	62%
Protamine	2%
Prothrombin complex concentrates	21%
Recombinant activated factor 7	2%

In bleeding patients with DIC and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), administration of fresh frozen plasma (FFP) may be useful

Important for me **Less important**



Fresh frozen plasma is correct. The clinical picture above is that of DIC. There is a prolongation of both PT and APTT. Patients with disseminated intravascular coagulopathy go through a hypercoagulable state followed by a hypo-coagulable state as they use up their reserves of clotting factors. Fresh frozen plasma replaces multiple clotting factors. The disturbed clotting state, as shown with prolongation of PT and APTT, indicates that clotting factor concentrations are below 30% of normal. A typical dose of fresh frozen plasma (15ml/kg) will increase circulating clotting factors by 10%.

Cryoprecipitate is incorrect because this is used to replace fibrinogen in haemorrhaging patients. It also contains Factor VIII and XIII, von Willebrand's Factor and fibronectin. It can be used in patients with von Willebrand's disease and haemophilia.

Protamine is incorrect because this is used to correct the effects of heparin, either unfractionated heparin or low molecular weight heparin. Administration can cause hypotension and high doses can inhibit platelet function.

Prothrombin complex concentrate is incorrect because this is used to reverse warfarin and can be used to reverse some direct oral anticoagulants. This includes clotting factors II, VII, IX and X. It is used for the rapid correction of an acquired coagulation disturbance, commonly warfarin. PT levels are monitored for dose-response. Repeat doses may be required 8-12 hours after the initial dose. An example is Octaplex.

Recombinant activated factor 7 is incorrect because this is used in haemophilia patients and off label in severe multiple trauma, non-traumatic intracranial haemorrhage and some surgeries. It is almost identical to native factor 7.



Discuss (1)

Improve

Next question >

Disseminated intravascular coagulation ★

Under homeostatic conditions, coagulation and fibrinolysis are coupled. The activation of the coagulation cascade yields thrombin that converts fibrinogen to fibrin; the stable fibrin clot being the final product of hemostasis. The fibrinolytic system breaks down fibrinogen and fibrin. Activation of the fibrinolytic system generates plasmin (in the presence of thrombin), which is responsible for the lysis of fibrin clots. The breakdown of fibrinogen and fibrin results in

polypeptides (fibrin degradation products). In a state of homeostasis, the presence of plasmin is critical, as it is the central proteolytic enzyme of coagulation and is also necessary for fibrinolysis.

In DIC, the processes of coagulation and fibrinolysis are dysregulated, and the result is widespread clotting with resultant bleeding. Regardless of the triggering event of DIC, once initiated, the pathophysiology of DIC is similar in all conditions. One critical mediator of DIC is the release of a transmembrane glycoprotein (tissue factor =TF). TF is present on the surface of many cell types (including endothelial cells, macrophages, and monocytes) and is not normally in contact with the general circulation, but is exposed to the circulation after vascular damage. For example, TF is released in response to exposure to cytokines (particularly interleukin 1), tumour necrosis factor, and endotoxin. This plays a major role in the development of DIC in septic conditions. TF is also abundant in tissues of the lungs, brain, and placenta. This helps to explain why DIC readily develops in patients with extensive trauma. Upon activation, TF binds with coagulation factors that then triggers the extrinsic pathway (via Factor VII) which subsequently triggers the intrinsic pathway (XII to XI to IX) of coagulation.

Causes of DIC

- sepsis
- trauma
- obstetric complications e.g. amniotic fluid embolism or hemolysis, elevated liver function tests, and low platelets (HELLP syndrome)
- malignancy

Diagnosis

A typical blood picture includes:

- ↓ platelets
- ↓ fibrinogen
- ↑ PT & APTT
- ↑ fibrinogen degradation products
- schistocytes due to microangiopathic haemolytic anaemia

Disorder	Prothrombin time	APTT	Bleeding time	Platelet count
Warfarin administration	Prolonged	Normal	Normal	Normal
Aspirin administration	Normal	Normal	Prolonged	Normal
Heparin	Often normal (may be prolonged)	Prolonged	Normal	Normal

Disorder	Prothrombin time	APTT	Bleeding time	Platelet count
DIC	Prolonged	Prolonged	Prolonged	Low

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Next question >

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Textbooks

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Media



Disseminated intravascular coagulation

Osmosis - YouTube

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A 45-year-old man is admitted from a local park. On arrival, he is in respiratory distress with a ventilatory rate of 34 breaths per minute and a peripheral oxygen saturation of 89% on 15L/min oxygen via a non-rebreathe mask. He is grey and sweaty with central cyanosis. Heart rate is 122bpm and blood pressure is 94/66mmHg. Examination of the chest discloses a normal cardiorespiratory examination and there is no clinical indication of heart failure. A chest x-ray shows no acute pathological lesion but background emphysematous changes and an ECG shows only sinus tachycardia with a corrected QT interval approaching the upper limit of normal with no ischaemic lesions.

An arterial blood gas taken on 15L/min oxygen shows:

pH	7.17	HCO ₃ ⁻	13.4	Glucose 6.9 mmol/l	MetHb	35%
pO ₂	10.9	Base excess	-5.8	Potassium 5.5 mmol/l	COHb	8%
pCO ₂	6.7	Lactate	4.1 mmol/l			

He is beginning to show signs of tiring and confusion and his GCS has fallen to 13/15 (E3V4M6) but he tells you he has been inhaling Liquid Gold (an alkyl nitrite).

Which of the following interventions is most appropriate in this patient's immediate management?

- ☐ Continuous positive airways pressure ventilation (CPAP) pending transfer to a hyperbaric chamber ×
- ☐ Reduce inspired oxygen concentration and controlled oxygen therapy via Venturi valve ×
- ☐ 75mg 1% methylthioninium chloride solution IV over 5 minutes ×
- ☐ 300mg 3% sodium nitrite solution IV over 10 minutes ×
- ☐ 50ml 8.4% sodium bicarbonate solution IV over 20 minutes ×

Submit answer

Reference ranges 

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A 45-year-old man is admitted from a local park. On arrival, he is in respiratory distress with a ventilatory rate of 34 breaths per minute and a peripheral oxygen saturation of 89% on 15L/min oxygen via a non-rebreathe mask. He is grey and sweaty with central cyanosis. Heart rate is 122bpm and blood pressure is 94/66mmHg. Examination of the chest discloses a normal cardiorespiratory examination and there is no clinical indication of heart failure. A chest x-ray shows no acute pathological lesion but background emphysematous changes and an ECG shows only sinus tachycardia with a corrected QT interval approaching the upper limit of normal with no ischaemic lesions.

An arterial blood gas taken on 15L/min oxygen shows:

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pO ₂	10.9	Base excess	-5.8	Potassium 5.5 mmol/l	COHb	8%
pCO ₂	6.7	Lactate	4.1 mmol/l			

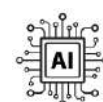
He is beginning to show signs of tiring and confusion and his GCS has fallen to 13/15 (E3V4M6) but he tells you he has been inhaling Liquid Gold (an alkyl nitrite).

Which of the following interventions is most appropriate in this patient's immediate management?

- Continuous positive airways pressure ventilation (CPAP) pending transfer to a hyperbaric chamber
5%
- Reduce inspired oxygen concentration and controlled oxygen therapy via Venturi valve
2%
- 75mg 1% methylthioninium chloride solution IV over 5 minutes
84%
- 300mg 3% sodium nitrite solution IV over 10 minutes
4%
- 50ml 8.4% sodium bicarbonate solution IV over 20 minutes
5%

Methylene blue can be used to treat methaemoglobinaemia. It causes a reduction of Fe³⁺ (ferric) to Fe²⁺ (ferrous)

Important for me Less important



The arterial blood gas in the above clinical description shows a mixed respiratory and metabolic acidosis with a relative hypoxia despite the inspired fraction of oxygen. However, the significant abnormality is the fraction of methaemoglobin on the gas at over 30% which is significantly elevated. The carboxyhaemoglobin level is slightly raised at 8% but levels such as this may be seen in smokers and are not necessarily pathological. In this case, the diagnosis is of acute methaemoglobinaemia which is a rare but potentially fatal consequence of inhalation of poppers (alkyl nitrites).

Poppers are a clear or yellowish, sweet-smelling volatile liquid which is inhaled as a recreational drug of abuse which yields euphoric and anxiolytic effects. It also is a vasodilator and is sometimes used as an adjunct in sexual acts, and previously was a treatment for angina pectoris. However, in some patients, particularly susceptible individuals such as those with sickle cell traits or a G6PD deficiency, inhalation of poppers may rapidly oxidise ferrous iron ions in haemoglobin to their ferric (Fe^{3+}) states creating methaemoglobinaemia (MetHb). MetHb binds oxygen more avidly than haemoglobin and causes a shift in the dissociation curve to the left meaning that oxygen is not liberated in the tissues causing a cellular hypoxia. This manifests in a clinical cyanosis and often a deathly grey pallor to the patient. Oxygen saturations may not be as shocking as the patient appears since many pulse oximeters cannot distinguish between oxyhaemoglobin and methaemoglobin well. However, supplemental oxygen will not improve recorded values (although it should still be given). An impairment in gas exchange is often seen in acute methaemoglobinaemia with raised tensions of CO_2 and low tension of O_2 and consequent respiratory acidosis. An additional metabolic acidosis occurs due to cellular anoxic respiration. In smokers, this condition may be mistaken for a type 2 respiratory failure due to chronic obstructive lung disease. The methaemoglobin count and low bicarbonate make this unlikely and reducing the inspired oxygen is likely to worsen the situation. CPAP may be tried but will not reverse the underlying problem and hyperbaric oxygen is helpful only in situations of high carboxyhaemoglobin, such as carbon monoxide poisoning, which is not the case here.

The first line treatment for methaemoglobinaemia is the administration of methylthioninium chloride, also known as methylene blue, which reduces the ferric ions back to their ferrous states rapidly. Several administrations may be required, especially in high concentrations of MetHb. Sodium nitrite is a recognised treatment for cyanide poisoning. It actually causes methaemoglobinaemia since cyanide ions are cleared more rapidly when complexed with MetHb. Administration of sodium nitrite is not indicated in this vignette and will make the situation worse. Sodium bicarbonate may well be indicated in this patient due to the profound acidosis but it is not the most pressing concern. Rectification of the oxygen-carrying capacity of the blood may improve the acid-base balance without the need for bicarbonate, and hypoxia is likely to kill the patient more quickly than acidosis with a normal potassium. Remember that 8.4% bicarbonate solution, if given, should ideally be infused through a central vein since it is extremely caustic.



Discuss (2)

Improve

Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapson, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO_2 but decreased oxygen saturation

Management

- NADH methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



123



Next question >

B

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A



T




Textbooks

High-yield textbook


Links

Life in the Fast Lane

 6  3

[Methaemoglobinaemia](#)

The Internet Book of Critical Care

 10  4

[Methemoglobinemia](#)



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Media







[Methaemoglobinaemia](#)

Osmosis - YouTube  7  2

[Report broken media](#)

Score: **12%**

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A 74-year-old gentleman presents with shortness of breath on exertion. He denies cough, wheeze, or chest pain. He has a past medical history of Hodgkin's lymphoma. Examination of the cardiopulmonary system is normal.

Blood results are as follows:

Hb	55 g/l
Platelets	346 * 10 ⁹ /l
WBC	8.4 * 10 ⁹ /l

You decide to transfuse him two units of red cells. What special request will you make?

- ☐ Leukodepleted ×
- ☐ CMV negative ×
- ☐ No special request required ×
- ☐ Irradiated red cells ×
- ☐ Cell salvage ×

Submit answer

Reference ranges 

Score: **0%**

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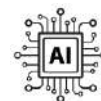
Hb	55 g/l
Platelets	$346 \times 10^9/l$
WBC	$8.4 \times 10^9/l$

You decide to transfuse him two units of red cells. What special request will you make?

Leukodepleted	9%
CMV negative	11%
No special request required	7%
Irradiated red cells	72%
Cell salvage	0%

The risk of transfusion associated graft versus host disease in Hodgkin's lymphoma is unrelated to the treatment modality and/or disease stage. Individuals with Hodgkin's lymphoma should therefore receive X- or gamma-irradiated blood for life

Important for me Less important



If an immunocompromised patient receives red cells that are not irradiated, the donor's T cells can cause transfusion-associated graft-versus-host disease (TA-GvHD), in which the donor T lymphocytes mount an immune response against the recipient's lymphoid tissue causing tissue and organ damage, potentially leading to death.

Typical clinical features of TA-GvHD include fever, an erythematous maculopapular rash, abdominal pain and profuse diarrhoea.

Irradiation of blood products destroys the donors T lymphocytes thereby helping to prevent this

potentially fatal complication.

Indications for gamma irradiated blood products include:

- Immunocompromised marrow or organ transplant recipients
- Patients with haematological disorders who will be undergoing allogeneic marrow transplantation imminently
- Intrauterine transfusions
- Patients with Hodgkin's disease
- Patients treated with purine analogue drugs (e.g. fludarabine)

Interestingly, the risk of transfusion associated graft versus host disease in Hodgkin's lymphoma is unrelated to the treatment modality and/or disease stage. Individuals with Hodgkin's lymphoma should therefore receive X- or gamma-irradiated blood for life.

In the UK, all blood products are leukodepleted to prevent Creutzfeldt-Jakob disease transmission.

The use of CMV-seronegative blood products is reserved for CMV-seronegative individuals that are likely to proceed to haematopoietic stem cell transplant, or neonates.

   Discuss (2)  Improve

Next question >

Blood products ★

Whole blood fractions

Fraction	Key points
Packed red cells	Used for transfusion in chronic anaemia and cases where infusion of large volumes of fluid may result in cardiovascular compromise. Product obtained by centrifugation of whole blood.
Platelet rich plasma	Usually administered to patients who are thrombocytopaenic and are bleeding or require surgery. It is obtained by low speed centrifugation.
Platelet concentrate	Prepared by high speed centrifugation and administered to patients with thrombocytopaenia.
Fresh frozen plasma	<ul style="list-style-type: none">• Prepared from single units of blood.• Contains clotting factors, albumin and immunoglobulin.• Unit is usually 200 to 250ml.

Fraction	Key points
	<ul style="list-style-type: none"> Usually used in correcting clotting deficiencies in patients with hepatic synthetic failure who are due to undergo surgery. Usual dose is 12-15ml/Kg⁻¹. It should not be used as first line therapy for hypovolaemia.
Cryoprecipitate	<ul style="list-style-type: none"> Formed from supernatant of FFP. Rich source of Factor VIII and fibrinogen. Allows large concentration of factor VIII to be administered in small volume.
SAG-Mannitol Blood	<p>Removal of all plasma from a blood unit and substitution with:</p> <ul style="list-style-type: none"> Sodium chloride Adenine Anhydrous glucose Mannitol <p>Up to 4 units of SAG M Blood may be administered. Thereafter whole blood is preferred. After 8 units, clotting factors and platelets should be considered.</p>

Cross matching

Must be cross matched	Can be ABO incompatible in adults
Packed red cells	Platelets
Fresh frozen plasma	
Cryoprecipitate	
Whole blood	

Cell saver devices

These collect patients own blood lost during surgery and then re-infuse it. There are two main types:

- Those which wash the blood cells prior to re-infusion. These are more expensive to purchase and more complicated to operate. However, they reduce the risk of re-infusing contaminated blood back into the patient.
- Those which do not wash the blood prior to re-infusion.

Their main advantage is that they avoid the use of infusion of blood from donors into patients and this may reduce risk of blood borne infection. It may be acceptable to Jehovah's witnesses. It is contraindicated in malignant disease for risk of facilitating disease dissemination.

Blood products used in warfarin reversal

In some surgical patients the use of warfarin can pose specific problems and may require the use of specialised blood products

Immediate or urgent surgery in patients taking warfarin(1) (2):

1. Stop warfarin

2. Vitamin K (reversal within 4-24 hours)

- IV takes 4-6h to work (at least 5mg)
- Oral can take 24 hours to be clinically effective

3. Fresh frozen plasma

- *Used less commonly now as 1st line warfarin reversal*
- 30ml/kg^{-1}
- Need to give at least 1L fluid in 70kg person (therefore not appropriate in fluid overload)
- Need blood group
- Only use if human prothrombin complex is not available

4. Human Prothrombin Complex (reversal within 1 hour)

- Bereplex 50 u/kg
- Rapid action but factor 6 short half life, therefore give with vitamin K



Next question >


B *I* **A** ▼ ▼ **T** ▼ ▼

Textbooks

High-yield textbook

Links

Life in the Fast Lane

 3  6

[Fresh Frozen Plasma \(FFP\)](#)

[Suggest link](#)

[Report broken link](#)

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Question 15 of 191



A 28-year-old woman presents to the acute medical unit with fatigue, lethargy, and abdominal pain. She is pregnant at 32 weeks gestation.

Blood results are as follows:

Hb	62 g/L	Male: (135-180) Female: (115 - 160)
Platelets	182 * 10 ⁹ /L	(150 - 400)
WBC	8.8 * 10 ⁹ /L	(4.0 - 11.0)

You discuss the case with the obstetrics registrar on call who advises you that they will review the patient in the department and asks you to arrange a blood transfusion.

What special red cell requirements are required?

- ☐ Cytomegalovirus (CMV) negative ×
- ☐ High titre anti-A and anti -B negative ×
- ☐ Irradiated ×
- ☐ Leukodepleted ×
- ☐ Washed ×

Submit answer

Reference ranges 

Score: **0%**

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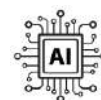
You discuss the case with the obstetrics registrar on call who advises you that they will review the patient in the department and asks you to arrange a blood transfusion.

What special red cell requirements are required?

Cytomegalovirus (CMV) negative	56%
High titre anti-A and anti -B negative	8%
Irradiated	21%
Leukodepleted	10%
Washed	5%

The use of CMV-seronegative blood products is reserved for CMV-seronegative individuals that are likely to proceed to haematopoietic stem cell transplant, or neonates

Important for me Less important



Cytomegalovirus (CMV) negative is the correct answer. CMV is a type of herpes virus. Primary infection is usually asymptomatic but may cause a flu or glandular fever-like illness, leading to a lifelong infection in all age groups. The virus resides in monocytes and can reactivate from its latent state. More severe disease may occur in individuals with impaired immunity such as foetuses, neonates and patients of any age who have been immuno-suppressed by disease or treatment.

Transmission of CMV present in blood components can give rise to primary infection in CMV-

negative patients or to reinfection in previously infected patients.

With very few stated exceptions (e.g. granulocytes), from November 1999 all allogeneic blood components produced in the UK have been subjected to a leukocyte depletion process. This was primarily a vCJD risk reduction measure, however, it has resulted in other added benefits including reduced incidence of non-febrile haemolytic transfusion reactions, TRALI, and transfer of CMV.

The following groups of patients require **CMV-negative blood**:

- Intra-uterine transfusions
- Neonates up to 28 days post expected date of delivery
- Pregnancy

As the patient in this clinical case is pregnant, CMV-negative blood is required.

Historically, immunocompromised patients who have not been infected with CMV (CMV negative) received CMV-negative blood due to the possible life-threatening complication of infection. However recent studies have shown that leukodepletion is just as effective as CMV IgG-negative blood components. Therefore CMV IgG negative donations are no longer required in this cohort.

Irradiated blood is required in individuals with severe immunodeficiencies, those with a history of Hodgkin's lymphoma, patients who have been exposed to certain drugs (e.g. bendamustine and fludarabine), and following stem cell transplant. Pregnancy is not an indication for irradiated blood.

All blood products in the UK are **leukodepleted** (with very few exceptions eg granulocytes). This is therefore not a special requirement.

With transfusion of plasma-rich components (e.g. FFP and platelets), we are more concerned about the passive transfer of antibodies (e.g. Anti-A and Anti-B) in contrast to the transfer of antigens as in red cell transfusions (which contain negligible amounts of plasma). Thus for plasma-rich components, group AB is the universal donor and group O is the universal recipient, in stark contrast to packed red cells. **High titre anti-A and anti -B** negative can be requested for incompatible plasma-rich transfusion. This clinical case is regarding red cell transfusions and thus this special requirement is not applicable.

Washed red cells can be requested for patients who have recurrent febrile or allergic reactions to standard packed red cells. Pregnancy is not an indication for washed red cells.

		 Discuss (2)	Improve
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Next question >

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Packed red cells	Platelets
Fresh frozen plasma	

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Cryoprecipitate	
Whole blood	

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- Oral can take 24 hours to be clinically effective

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- *Used less commonly now as 1st line warfarin reversal*
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- Need to give at least 1L fluid in 70kg person (therefore not appropriate in fluid overload)
- Need blood group
- Only use if human prothrombin complex is not available

4. Human Prothrombin Complex (reversal within 1 hour)

- Bereplex 50 u/kg
- Rapid action but factor 6 short half life, therefore give with vitamin K



123

[Next question >](#)**B***I***A****T**

Textbooks

[High-yield textbook](#)[Extended textbook](#)

Links

[Life in the Fast Lane](#)

3



6

[Fresh Frozen Plasma \(FFP\)](#)[Suggest link](#)[Report broken link](#)Score: **12%**

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A 35-year-old man presents to the emergency department with generalised weakness, nausea, and joint pain. He has a past medical history of depression for which he has been prescribed sertraline but has not taken it for several months. He is a current smoker and also uses intravenous recreational drugs.

On examination, he has a non-blanching, slightly raised purplish rash over his torso and part of his limbs. He is slightly jaundiced and has mild right upper quadrant tenderness.

Blood tests are taken:

Bilirubin	51 µmol/L	(3 - 17)
ALP	188 u/L	(30 - 100)
ALT	142 u/L	(3 - 40)
Î³GT	82 u/L	(8 - 60)
Albumin	29 g/L	(35 - 50)
HBsAg	Negative	
Anti-HBV	Negative	
Anti-HCV	Positive	
HCV RNA	Positive	
HIV antibodies	Negative	

What is the most likely diagnosis?

- ☐ Cold agglutinin disease ×
- ☐ Cryoglobulinaemia type 1 ×
- ☐ Cryoglobulinaemia type 2 ×
- ☐ Cryoglobulinaemia type 3 ×
- ☐ Warm autoimmune haemolytic anaemia ×

Submit answer

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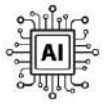
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Albumin	29 g/L	(35 - 50)
HBsAg	Negative	
Anti-HBV	Negative	
Anti-HCV	Positive	
HCV RNA	Positive	
HIV antibodies	Negative	

What is the most likely diagnosis?

Cold agglutinin disease	2%
Cryoglobulinaemia type 1	21%
Cryoglobulinaemia type 2	66%
Cryoglobulinaemia type 3	8%
Warm autoimmune haemolytic anaemia	3%

Hepatitis C + purpuric rash → cryoglobulinaemia

Important for me Less important



This patient, in summary, has generalised weakness, arthralgia, and a rash consistent with palpable purpura on the background of a diagnosis of hepatitis C. The combination of hepatitis C and purpura is suspicious of cryoglobulinaemia. Meltzer's triad is a combination of palpable purpura, arthralgia, and weakness and are the classical symptoms of cryoglobulinaemia.

There are three types of cryoglobulinaemia. It is **cryoglobulinaemia type 2** that is associated with hepatitis C and therefore this is the correct answer. Other associations of type 2 include rheumatoid arthritis, Sjogren's, and lymphoma.

Cold agglutinin disease is an autoimmune disease caused by the presence of cold-sensitive antibodies which act on red blood cells. It has both primary and secondary forms, of which hepatitis C can be a trigger of secondary cold agglutinin disease. Symptoms can include arthralgia and weakness, but the presence of palpable purpura is not associated. Therefore, this diagnosis is less likely.

Cryoglobulinaemia type 1 is not associated with hepatitis C. Associations include multiple myeloma and Waldenstrom macroglobulinaemia.

Cryoglobulinaemia type 3 is not associated with hepatitis C. Associations include rheumatoid arthritis and Sjogren's.

Warm autoimmune haemolytic anaemia is the most common form of autoimmune anaemia. It is idiopathic in 50% of cases. In others, it is often associated with another autoimmune disease such as rheumatoid arthritis or systemic lupus erythematosus. Therefore, this diagnosis is unlikely in this case.

		Discuss (1)	Improve
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Next question >

Cryoglobulinaemia ★

Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C. One-third of cases are idiopathic

Three types

- type I (25%):
 - monoclonal - IgG or IgM
 - associations: multiple myeloma, Waldenstrom macroglobulinaemia
- type II (25%)
 - mixed monoclonal and polyclonal: usually with rheumatoid factor
 - associations: **hepatitis C**, rheumatoid arthritis, Sjogren's, lymphoma

- type III (50%)
 - polyclonal: usually with rheumatoid factor
 - associations: rheumatoid arthritis, Sjogren's

Possible features

- Raynaud's only seen in type I
- cutaneous
 - vascular purpura
 - distal ulceration
 - ulceration
- arthralgia
- renal involvement
 - diffuse glomerulonephritis

Investigations

- low complement (esp. C4)
- high ESR

Management

- treatment of underlying condition e.g. hepatitis C
- immunosuppression
- plasmapheresis



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Score: **12%**

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A 40-year-old man presents to the Emergency Department with non-specific symptoms of lethargy, malaise, headache, body aches, a low-grade fever and a sore throat. The examination is essentially normal aside from multiple limb petechiae. Tympanic temperature is 37.6°C. Blood pressure, heart rate and pulse oximetry are normal.

Blood tests show:

Haemoglobin	112g/L	Sodium	136mmol/L
MCV	82fL	Potassium	4.5mmol/L
Platelets	$77 \times 10^9/L$	Urea	6.9mmol/L
White cells	$32 \times 10^9/L$	Creatinine	111 μ mol/L
Prothrombin time	23secs	CRP	54mg/L
Fibrinogen	0.45g/L	HIV test	Negative
Liver enzymes	normal		

The automated counter is unable to supply differential white cell count.

Manual blood film shows immature granulocytes with bilobed nuclei and Auer rods.

What is the most important immediate therapy to institute?

- ☐ All trans retinoic acid (ATRA) [tretinoin] ×
- ☐ Methotrexate ×
- ☐ Imatinib ×
- ☐ Rituximab ×
- ☐ Arsenic trioxide ×

Submit answer

Reference ranges ∨

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Liver enzymes	normal		

The automated counter is unable to supply differential white cell count.

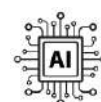
Manual blood film shows immature granulocytes with bilobed nuclei and Auer rods.

What is the most important immediate therapy to institute?

All trans retinoic acid (ATRA) [tretinoin]	74%
Methotrexate	1%
Imatinib	15%
Rituximab	9%
Arsenic trioxide	1%

APML is treated with all-trans retinoic acid (ATRA) to force immature granulocytes into maturation to resolve a blast crisis prior to more definitive chemotherapy

Important for me Less important



The above vignette gives a classical description of acute promyelocytic leukaemia (APML). This diagnosis is considered a haematological emergency. Approximately 10% of patients with an acute leukaemia are ultimately diagnosed with APML but it is a largely unconsidered diagnosis. If diagnosed, it is one of the most treatable leukaemias, however, in one-third of cases the initial presentation is of catastrophic haemorrhage.

The average age of presentation with APML is 30-40 which distinguishes it from other acute myeloid leukaemias which present in the seventh decade typically. Other presenting symptoms are similar however with fatigue and weakness due to anaemia, coryzal or influenza symptoms and easy bruising due to thrombocytopaenia and coagulopathy. Myeloid leukaemia may cause splenomegaly which is usually absent in APML. Lymphadenopathy does not occur in leukaemias of myeloid line.

A blood film may show characteristic Auer rods in both myeloid leukaemia and APML. The film will show abnormal myeloid precursor cells or granulocytes in APML which are often bilobar or multilobar, whereas leukaemic mature myeloid cells are present in other forms of myeloid leukaemia although distinguishing these is difficult. Automated counters may fail to determine a differential white cell count. Confirmation of APML is via polymerase chain reaction or fluorescent in-situ hybridisation (FISH) of the bone marrow which demonstrates translocation of chromosomes 15 and 17. A gene on chromosome 17 codes for the retinoic acid receptor alpha protein and in APML patients with this translocation, administration of all-trans retinoic acid forces the immature myeloid cell to mature and it then undergoes apoptosis. ATRA is considered an emergency treatment for an APML blast crisis in those with coagulopathy or severe anaemia or sepsis. ATRA is considered only an emergency drug to force cell maturation; ongoing chemotherapy is required to maintain remission. Current guidelines recommend arsenic trioxide as the first line agent to achieve remission once ATRA therapy is commenced and also in refractory disease.

Methotrexate may sometimes be used to maintain remission in some APML patients although it is not helpful in the acute presentation.

Imatinib is a tyrosine kinase inhibitor used in the treatment of chronic myeloid leukaemia, particularly those with the Philadelphia translocation. It is not commonly used in this scenario.

Rituximab is a monoclonal antibody against CD20 on B cells. It has many uses in inflammatory diseases, lymphoma and lymphocytic leukaemia but is rarely used in APML or myeloid leukaemia (since B cells are of lymphoid, not myeloid lineage). There are some studies which have suggested a link between rituximab usage and the development of APML.

		 Discuss	Improve
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Next question >

You are not normally expected to be able to differentiate the different subtypes of acute myeloid leukaemia (AML) for the MRCP. An exception to this is acute promyelocytic leukaemia (APML, the M3 subtype of AML). The importance of identifying APML lies in both the presentation (classically disseminated intravascular coagulation) and management

APML is associated with the t(15;17) translocation which causes fusion of the PML and RAR-alpha genes.

Features

- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

APML is treated with all-trans retinoic acid (ATRA) to force immature granulocytes into maturation to resolve a blast crisis prior to more definitive chemotherapy.



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Score: **12%**

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A 43-year-old man presents to the emergency department with melaena and haematemesis. He has a past medical history of immune thrombocytopenia and is not currently on any treatment. He does not drink alcohol.

Observations:

- Heart rate 108 beats per minute
- Blood pressure 92/58 mmHg
- Respiratory rate 18/minute
- Oxygen saturations 96% on room air
- Temperature 37.1°C

On examination, there is dried blood around the patient's mouth. Ecchymoses are noted on his arms and abdomen. There is melaena per rectum. There are no signs of chronic liver disease.

Blood tests:

Hb	73 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$9 \times 10^9/L$	(150 - 400)
WBC	$8.2 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	137 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	89 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	12 µmol/L	(3 - 17)
ALP	38 u/L	(30 - 100)
ALT	27 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	38 g/L	(35 - 50)
Prothrombin time	11 seconds	(10-12)

Given the clinical history, what is the most appropriate choice of treatment to raise the platelet

count?

<input type="radio"/>	Azathioprine	×
<input type="radio"/>	Intravenous immunoglobulin	×
<input type="radio"/>	Prednisolone	×
<input type="radio"/>	Rituximab	×
<input type="radio"/>	Romiplostin	×

Submit answer

Reference ranges ▾

Score: 0%

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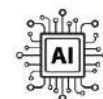
Given the clinical history, what is the most appropriate choice of treatment to raise the platelet

count?

Azathioprine	0%
Intravenous immunoglobulin	64%
Prednisolone	32%
Rituximab	1%
Romiplostin	3%

Human immunoglobulin (IVIG) is an alternative to steroids in treating ITP, particularly if the platelets need to be raised quickly

Important for me Less important



Intravenous immunoglobulin (IVIG) is correct. The patient presents with life-threatening bleeding and a platelet count of 9. The fastest way to increment the platelet count in ITP is with IVIG, which is indicated in cases of life-threatening bleeding. The expected response time is 1-3 days. In cases of life-threatening bleeding, platelets are typically given in addition.

Prednisolone is incorrect. This is the typical first-line treatment for ITP. However, in cases of life-threatening bleeding and where the platelet count needs to be incremented quickly, IVIG is more effective. The expected response time is 4-14 days.

Rituximab is incorrect. This is used in refractory cases and takes between 7-56 days to raise the platelet count. It would not be used in the first instance.

Azathioprine is incorrect. This can be used as a steroid-sparing agent in ITP but it takes between 30-90 days to work and would therefore not be used in an emergency such as this case.

Romiplostin is incorrect. This is a fusion protein that activates the thrombopoietin (TPO) receptor and increases platelet production. It takes between 5-14 days to raise the platelet count.

Discuss (2) [Improve](#)

[Next question >](#)

Immune thrombocytopenia (ITP) in adults ★

Immune (or idiopathic) thrombocytopenic purpura (ITP) is an immune-mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb/IIIa or Ib-V-IX complex.

Children with ITP usually have an acute thrombocytopenia that may follow infection or vaccination. In contrast, adults tend to have a more chronic condition.

ITP in adults

Epidemiology

- more common in older females

Presentation

- may be detected incidentally following routine bloods
- symptomatic patients may present with
 - petechiae, purpura
 - bleeding (e.g. epistaxis)
 - catastrophic bleeding (e.g. intracranial) is not a common presentation

Investigations

- full blood count: isolated thrombocytopenia
- blood film
- a bone marrow examination is no longer used routinely
- antiplatelet antibody testing has poor sensitivity and doesn't affect clinical management so is not commonly done

Management

- first-line treatment for ITP is oral prednisolone
- pooled normal human immunoglobulin (IVIG) may also be used
 - it raises the platelet count quicker than steroids, therefore may be used if active bleeding or an urgent invasive procedure is required
- splenectomy is now less commonly used

Evan's syndrome

- ITP in association with autoimmune haemolytic anaemia (AIHA)



+

Q

123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

👍 14 🗑️ 7

[2003 ITP guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Bleeding Disorders \(ITP vs TTP vs HUS vs DIC\)](#)

Dirty USMLE - YouTube

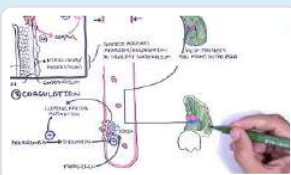
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[Immune thrombocytopenia \(ITP\)](#)

Osmosis - YouTube

👍 4 🗑️ 0



[Thrombocytopaenia \(low platelets\) Overview - platelet physiology, classification, pathophysiology](#)

Armando Hasudungan - YouTube

👍 2 🗑️ 1

[Report broken media](#)

Score: **12%**

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A 36-year-old female was referred to the outpatient haematology clinic having been referred by her GP with a falling white cell count. Eight weeks ago she saw her own GP complaining of feeling continuously tired after a viral upper respiratory illness two weeks prior to the onset of her symptoms. She also complained of feeling generally unwell and of having intermittent pains in all her joints and muscles without swelling or stiffness. Her respiratory symptoms had fully resolved and she denied any night sweats or weight loss. Her GP organised a set of screening blood investigations which revealed a white cell count of 2.6×10^9 g/dl (neutrophil count 2.0×10^9 g/dl). This was repeated on two further occasions over the next four weeks revealing results of 2.2 and 1.9 respectively (neutrophil counts of 1.5×10^9 g/dl and 1.2×10^9 g/dl respectively). Her past medical history included hypothyroidism for which she was treated with levothyroxine 150mcg OD.

Examination at the clinic revealed the presence of a systemically well female. Her blood pressure was 118/74 mmHg, heart rate 82 bpm, respiratory rate 16/min and temperature 36.6°C. Examination of her cardiovascular system was unremarkable. Similarly, examination of her gastrointestinal system was unremarkable, with no organomegaly identified. No cervical, axillary or inguinal lymph nodes were palpable. Examination of her ENT system was unremarkable.

Initial investigations at the clinic revealed the following results:

Hb	122 g/l
WCC	2.0×10^9 /l
Neutrophils	1.3×10^9 /l
Lymphocytes	0.6×10^9 /l
Monocytes	0.1×10^9 /l
Platelets	224×10^9 /l
Blood film	neutropaenia
B12	224 (NR 160-900 ng/l)
ESR	15 mm/hr
CRP	9 mg/l
TSH	0.35 (NR 0.4-3.6mu/ml)
FT4	11.6 (NR 4.5-13.6 mcg/dl)
Monospot test	negative
CMV serology	negative

What is the single most appropriate management option?

- ☐ Organise bone marrow aspirate and biopsy
- ☐ Organise peripheral blood flow cytometry analysis
- ☐ Repeat full blood count in four weeks
- ☐ Organise CT neck, thorax, abdomen and pelvis
- ☐ Organise blood cytogenetic analysis

Submit answer

Reference ranges

Score: 0%

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FT4	11.6 (NR 4.5-13.6 mcg/dl)
Monospot test	negative
CMV serology	negative

What is the single most appropriate management option?

Organise bone marrow aspirate and biopsy

28%

Organise peripheral blood flow cytometry analysis

24%

Repeat full blood count in four weeks

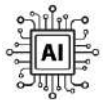
38%

Organise CT neck, thorax, abdomen and pelvis

3%

Organise blood cytogenetic analysis

8%



This is a very common scenario seen in the haematology outpatient clinic. This patient most probably has transient myelosuppression secondary to a viral infection with post viral fatigue and malaise. Although she is symptomatic, she is systemically well and there are no other red flag symptoms or signs including the presence of lymphadenopathy and splenomegaly. Her neutrophil count has been falling but it has remained above 1 and she is not febrile or septic. Her neutrophil count is beginning to improve (albeit very slowly) and therefore a repeat FBC would be justified to ensure that it does return to normal. If it remains low further investigation would be justified.



Discuss (13)

Improve

Next question >

Neutropaenia ★

Neutropaenia refers to a low neutrophil counts, $< 1.5 \times 10^9$. A normal neutrophil count is $2.0 - 7.5 \times 10^9$.

It is important to recognise as it predisposes to severe infection.

Neutropaenia may be further subdivided as follows:

Severity	Neutrophil count
Mild	$1.0 - 1.5 \times 10^9$
Moderate	$0.5 - 1.0 \times 10^9$
Severe	$< 0.5 \times 10^9$

Causes

- viral
 - HIV
 - Epstein-Barr virus
 - hepatitis
- drugs
 - cytotoxics
 - carbimazole
 - clozapine
- benign ethnic neutropaenia
 - common in people of black African and Afro-Caribbean ethnicity
 - requires no treatment
- haematological malignancy
 - myelodysplastic malignancies
 - aplastic anemia
- rheumatological conditions
- systemic lupus erythematosus: mechanisms include circulating antineutrophil antibodies
- rheumatoid arthritis: e.g. hypersplenism as in Felty's syndrome
- severe sepsis
- haemodialysis



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Score: **12%**

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You are asked to review a 74-year-old man on the haematology ward. He complains of widespread bruising and bleeding gums. He has a past medical history of myelodysplasia. He has required 6 red cell transfusion and 5 platelet transfusions in the past 12 months.

Blood results are as follows:

Hb	95 g/l
Platelets	$8 \times 10^9/l$
WBC	$4.2 \times 10^9/l$

You decide to transfuse him 1 unit of platelets. A repeat blood test the following day is reported below:

Hb	92 g/l
Platelets	$12 \times 10^9/l$
WBC	$3.8 \times 10^9/l$

What investigation will you order next?

- ☐ Anti HLA antibodies ×
- ☐ Platelet Factor 4 Antibody ×
- ☐ Von Willebrand factor (vWF) levels ×
- ☐ Lupus anticoagulant ×
- ☐ Anti- $\beta 2$ glycoprotein ×

Submit answer

Reference ranges 

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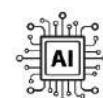
Hb	92 g/l
Platelets	$12 \times 10^9/l$
WBC	$3.8 \times 10^9/l$

What investigation will you order next?

Anti HLA antibodies	26%
Platelet Factor 4 Antibody	47%
Von Willebrand factor (vWF) levels	12%
Lupus anticoagulant	2%
Anti- $\beta 2$ glycoprotein	12%

HLA-matched platelets and single-donor platelets are used for individuals that are refractory to platelet transfusions and have developed anti-HLA or antiplatelet antibodies

Important for me Less important







Platelet refractoriness is a failure to obtain a satisfactory response to a platelet transfusion on two or more occasions. An unsatisfactory response is defined by a platelet rise of less than $10 \times 10^9/l$.

When a patient does not have a satisfactory response to a platelet transfusion it is important to establish exactly why this has occurred. There are many mechanisms which can play a role including both immunological (e.g. alloimmunisation) and non-immunological (e.g. splenomegaly, DIC and sepsis).

This patient has had multiple previous platelet transfusions, making alloimmunisation high up in the differential. It is therefore important to check for anti-HLA or antiplatelet antibodies. HLA-matched platelets and single-donor platelets are used for individuals that are refractory to platelet transfusions and have developed anti-HLA or antiplatelet antibodies.

Platelet Factor 4 (PF4) antibodies are checked when heparin induced thrombocytopenia is suspected.

Anti- β 2 glycoprotein and lupus anticoagulant are checked when antiphospholipid syndrome is suspected.

   Discuss (5)  Improve

Next question >

Blood products ★

Whole blood fractions

Fraction	Key points
Packed red cells	Used for transfusion in chronic anaemia and cases where infusion of large volumes of fluid may result in cardiovascular compromise. Product obtained by centrifugation of whole blood.
Platelet rich plasma	Usually administered to patients who are thrombocytopaenic and are bleeding or require surgery. It is obtained by low speed centrifugation.
Platelet concentrate	Prepared by high speed centrifugation and administered to patients with thrombocytopaenia.

Fraction	Key points
Fresh frozen plasma	<ul style="list-style-type: none"> • Prepared from single units of blood. • Contains clotting factors, albumin and immunoglobulin. • Unit is usually 200 to 250ml. • Usually used in correcting clotting deficiencies in patients with hepatic synthetic failure who are due to undergo surgery. • Usual dose is 12-15ml/Kg⁻¹. • It should not be used as first line therapy for hypovolaemia.
Cryoprecipitate	<ul style="list-style-type: none"> • Formed from supernatant of FFP. • Rich source of Factor VIII and fibrinogen. • Allows large concentration of factor VIII to be administered in small volume.
SAG-Mannitol Blood	<p>Removal of all plasma from a blood unit and substitution with:</p> <ul style="list-style-type: none"> • Sodium chloride • Adenine • Anhydrous glucose • Mannitol <p>Up to 4 units of SAG M Blood may be administered. Thereafter whole blood is preferred. After 8 units, clotting factors and platelets should be considered.</p>

Cross matching

Must be cross matched	Can be ABO incompatible in adults
Packed red cells	Platelets
Fresh frozen plasma	
Cryoprecipitate	
Whole blood	

Cell saver devices

These collect patients own blood lost during surgery and then re-infuse it. There are two main types:

- Those which wash the blood cells prior to re-infusion. These are more expensive to purchase and more complicated to operate. However, they reduce the risk of re-infusing contaminated blood back into the patient.

- Those which do not wash the blood prior to re-infusion.

Their main advantage is that they avoid the use of infusion of blood from donors into patients and this may reduce risk of blood borne infection. It may be acceptable to Jehovah's witnesses. It is contraindicated in malignant disease for risk of facilitating disease dissemination.

Blood products used in warfarin reversal

In some surgical patients the use of warfarin can pose specific problems and may require the use of specialised blood products

Immediate or urgent surgery in patients taking warfarin(1) (2):

1. Stop warfarin

2. Vitamin K (reversal within 4-24 hours)

- IV takes 4-6h to work (at least 5mg)
- Oral can take 24 hours to be clinically effective

3. Fresh frozen plasma

- *Used less commonly now as 1st line warfarin reversal*
- 30ml/kg^{-1}
- Need to give at least 1L fluid in 70kg person (therefore not appropriate in fluid overload)
- Need blood group
- Only use if human prothrombin complex is not available

4. Human Prothrombin Complex (reversal within 1 hour)

- Bereplex 50 u/kg
- Rapid action but factor 6 short half life, therefore give with vitamin K



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

Life in the Fast Lane

 3  6

[Fresh Frozen Plasma \(FFP\)](#)

[Suggest link](#)

[Report broken link](#)

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The hospital is running low on its stock of cytomegalovirus (CMV) seronegative blood products. All the blood products are routinely leuko-depleted to reduce the risk of transferring CMV. You are asked to prioritise patients for CMV seronegative blood.

From the following options, which patient is the highest priority?

- ☐ Patient having post-partum haemorrhage after delivery of twins

×
- ☐ Patient on high dose oral steroids for temporal arteritis

×
- ☐ Patient with HIV with CD4 count 50, not on anti-retroviral therapy

×
- ☐ Patient with acute myeloid leukaemia who is planned for haematopoietic stem cell transplant next week

×
- ☐ Patient with previous CMV pneumonitis

×

Submit answer

Reference ranges ▾

Score: 0%

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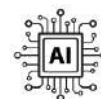
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From the following options, which patient is the highest priority?

Patient having post-partum haemorrhage after delivery of twins	19%
Patient on high dose oral steroids for temporal arteritis	1%
Patient with HIV with CD4 count 50, not on anti-retroviral therapy	19%
Patient with acute myeloid leukaemia who is planned for haematopoietic stem cell transplant next week	58%
Patient with previous CMV pneumonitis	4%

The use of CMV-seronegative blood products is reserved for CMV-seronegative individuals that are likely to proceed to haematopoietic stem cell transplant, or neonates

Important for me Less important



The correct answer is patient 4 who is planning for a haematopoietic stem cell transplant. The patient with the post-partum haemorrhage and the patient with severe anaemia secondary to upper GI bleed both require emergency transfusion but do not require CMV negative blood.

Other patients that should receive CMV-negative blood are neonates and pregnant women (other than during delivery). Blood from a patient who is seropositive for CMV is potentially infectious to the recipient due to either infectious virus in the plasma or latent virus in the monocytes in the blood. Blood products are leuko-depleted to remove the white blood cells to reduce the risk of transmission via monocytes. The use of seronegative blood has a lower risk of transfer to CMV but there is still a possible risk of transmission, as the antibodies take time to become positive after the donor has been infected.

Post-partum haemorrhage: pregnant women should be given seronegative blood if possible during pregnancy to prevent CMV infection of the fetus. This does not apply during or after delivery because there is no risk to the fetus, so this patient would not require seronegative blood.

High-dose oral steroids: this patient does not require seronegative blood because immune suppression is not an indication for seronegative blood products.

HIV infection is not an indication for seronegative blood products even in advanced untreated disease.

Previous CMV pneumonitis: this patient has already been infected with CMV and therefore does not require seronegative blood products.



Discuss (3)

Improve

Next question >

Blood products ★

Whole blood fractions

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Packed red cells	Used for transfusion in chronic anaemia and cases where infusion of large volumes of fluid may result in cardiovascular compromise. Product obtained by centrifugation of whole blood.
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123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

Life in the Fast Lane

3 6

Fresh Frozen Plasma (FFP)

[Suggest link](#)

[Report broken link](#)

Score: **12%**

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A 23-year-old man presents with diffuse bruising, abdominal pain, and loss of appetite. He feels unwell and has no history of taking any medications, does not use dietary supplements, and does not use illicit drugs. His past medical history is negative for any prior illnesses or hospitalisations. No family history of any bleeding disorders.

On examination, he has a heart rate of 115 bpm with a blood pressure of 130/75mmHg. His respiratory rate is 18 breaths per minute and he is afebrile with a temperature of 37.2°C. His abdominal exam demonstrates rebound tenderness in the right lower quadrant.

Investigations:

Hb	13.7 g/L	(135-180)
Platelets	48 * 10 ⁹ /L	(150 - 400)
WBC	5 * 10 ⁹ /L	(4.0 - 11.0)
Haematocrit	41%	(41-50%)
INR	1.1	(0.9-1.2)
Fibrinogen	2.2 g/L	(2 - 4)

A diagnosis of acute appendicitis is made and the general surgical team decides that the patient needs to be taken to theatre for an urgent laparoscopic appendectomy.

What is the next best step in his management?

- ☐ Antithymocyte globulin plus ciclosporin ×
- ☐ Give intravenous glucocorticoid ×
- ☐ Haematopoietic stem cell transplant ×
- ☐ Start intravenous human immunoglobulin ×
- ☐ Urgent platelet transfusion ×

Submit answer

Reference ranges ∨

Score: **0%**

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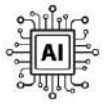
A diagnosis of acute appendicitis is made and the general surgical team decides that the patient needs to be taken to theatre for an urgent laparoscopic appendectomy.

What is the next best step in his management?

Antithymocyte globulin plus ciclosporin	1%
Give intravenous glucocorticoid	10%
Haematopoietic stem cell transplant	1%
Start intravenous human immunoglobulin	48%
Urgent platelet transfusion	40%

Human immunoglobulin (IVIG) is an alternative to steroids in treating ITP, particularly if the platelets need to be raised quickly

Important for me Less important



Primary immune thrombocytopenia (ITP, also called idiopathic thrombocytopenic purpura, immune thrombocytopenic purpura) is acquired thrombocytopenia caused by autoantibodies against platelet antigens leading to platelet destruction and platelet underproduction that is not triggered by an apparent associated condition. The likely diagnosis is ITP here as the patient has normal white cell counts and haemoglobin, no other causes of coagulopathy with normal PT/INR, no family history of bleeding disorder and clinically no organomegaly.

IVIg can raise the platelet count within 12 to 24 hours in many patients with ITP; this effect is reproducible enough that a platelet count response to IVIg has been used as a diagnostic criterion for ITP. The effect of IVIg usually persists for two to six weeks. Thus, IVIg is most useful for patients who require a rapid, temporary increase in platelet count (for urgent management of bleeding associated with thrombocytopenia or before an urgent invasive procedure) or those who are unable to tolerate glucocorticoids and are awaiting initiation of second-line therapy.

IV glucocorticoid therapy is incorrect as it's not preferred therapy in this situation where there is a need for urgent surgery. IVIg may be used either as an adjunct to other therapies in an individual with critical bleeding or need for urgent surgery or as an alternative to glucocorticoids in patients with severe bleeding.

Urgent platelet transfusion will be an ineffective treatment in immune (idiopathic) thrombocytopenic purpura especially when planning for immediate surgery as it is controversial, as transfused platelets are short-lived and platelet transfusion has been linked to arterial thrombosis and mortality in platelet consumptive disorders like ITP.

Antithymocyte globulin plus ciclosporin is not the right option for treatment here as it is used in immune-mediated aplastic anaemia.

Haematopoietic stem cell transplant is not applicable in this situation as it is the best treatment for young patients with aplastic anaemia with the best match available.

		Discuss (7)	Improve
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Next question >

Immune thrombocytopenia (ITP) in adults ★

Immune (or idiopathic) thrombocytopenic purpura (ITP) is an immune-mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb/IIIa or Ib-V-IX complex.

Children with ITP usually have an acute thrombocytopenia that may follow infection or vaccination. In contrast, adults tend to have a more chronic condition.

ITP in adults

Epidemiology

- more common in older females

Presentation

- may be detected incidentally following routine bloods
- symptomatic patients may present with
 - petechiae, purpura
 - bleeding (e.g. epistaxis)
 - catastrophic bleeding (e.g. intracranial) is not a common presentation

Investigations

- full blood count: isolated thrombocytopenia
- blood film
- a bone marrow examination is no longer used routinely
- antiplatelet antibody testing has poor sensitivity and doesn't affect clinical management so is not commonly done

Management

- first-line treatment for ITP is oral prednisolone
- pooled normal human immunoglobulin (IVIG) may also be used
 - it raises the platelet count quicker than steroids, therefore may be used if active bleeding or an urgent invasive procedure is required
- splenectomy is now less commonly used

Evan's syndrome

- ITP in association with autoimmune haemolytic anaemia (AIHA)



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Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

 14  7

[2003 ITP guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Bleeding Disorders \(ITP vs TTP vs HUS vs DIC\)](#)


Dirty USMLE - YouTube

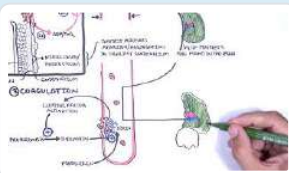
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[Immune thrombocytopenia \(ITP\)](#)



Osmosis - YouTube

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[Thrombocytopaenia \(low platelets\) Overview - platelet physiology, classification, pathophysiology](#)

Armando Hasudungan - YouTube

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[Report broken media](#)

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A 56-year-old woman presents with lethargy and vomiting to her GP. She is normally fit and well. Blood tests and a urine sample are sent.

Hb	110 g/L ⁹ /L	Female: (115 - 160)
Platelets	160 * 10 ⁹ /L	(150 - 400)
WBC	5 * 10 ⁹ /L	(4.0 - 11.0)

Na ⁺	132 mmol/L	(135 - 145)
K ⁺	4.8 mmol/L	(3.5 - 5.0)
Urea	11.1 mmol/L	(2.0 - 7.0)
Creatinine	140 µmol/L	(55 - 120)

Calcium	3.0 mmol/L	(2.1-2.6)
Phosphate	1.2 mmol/L	(0.8-1.4)
Magnesium	0.8 mmol/L	(0.7-1.0)

Urine electrophoresis is positive for Bence Jones protein.

Given the likely underlying diagnosis, what imaging is recommended to assess for bony involvement?

☐ DEXA scan
 ×

☐ Isotope bone scan
 ×

☐ No imaging required at diagnosis
 ×

☐ Whole body MRI
 ×

☐ X-rays of spine and pelvis
 ×

Submit answer

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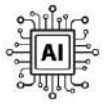
Given the likely underlying diagnosis, what imaging is recommended to assess for bony involvement?

DEXA scan	2%
Isotope bone scan	6%
No imaging required at diagnosis	2%
Whole body MRI	86%
X-rays of spine and pelvis	5%

Whole body MRI 1st line imaging in suspected multiple myeloma

Important for me

Less important



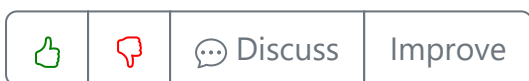
The presence of hypercalcaemia, acute kidney injury and Bence Jones proteins in the urine is highly suggestive of a diagnosis of multiple myeloma. In their 2016 guidelines, NICE recommends whole-body imaging at diagnosis of multiple myeloma to assess for bony involvement. They recommend whole-body MRI as first line. Whole-body CT or positron emission tomography (PET) scans can be used as alternatives if MRI is inappropriate or unavailable. The other options are not recommended as first-line imaging modalities in this circumstance by NICE.

A DEXA scan is used in combination with a FRAX tool assessment to assess for future fracture risk in patients with known or suspected osteoporosis.

Nuclear medicine scans such as an isotope bone scan are not recommended as first-line imaging in this situation. Some indications for isotope bone scans include investigating for Paget's disease, osteomyelitis or in primary bone malignancies.

In their 2016 guidelines, NICE recommends whole-body imaging at the time of diagnosis of myeloma to assess for bony involvement.

X-rays can show typical lytic lesions associated with bony involvement in myeloma. However, X-rays are inadequate to exclude bony involvement and are therefore not recommended as first-line imaging in this circumstance.



Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells

- much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
- this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



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Next question >

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T



Textbooks

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Extended textbook


Links

Clinical Knowledge Summaries

 10  10

[Haematological cancers - recognition and referral](#)

NICE

 12  6

[2016 myeloma guidelines](#)

[Suggest link](#)



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Media



[Multiple Myeloma - Diagnosis and Treatment](#)



Medicosis Perfectionalis - YouTube

 6  0



[Multiple Myeloma](#)

Medicosis Perfectionalis - YouTube

 4  0



[Multiple Myeloma Mnemonic...the story of the plasma cell](#)

Medicosis Perfectionalis - YouTube

 5  1



What is multiple myeloma?

Khan Academy - YouTube

👍 4 🗨️ 1



Multiple Myeloma

Townsend Teaching - YouTube

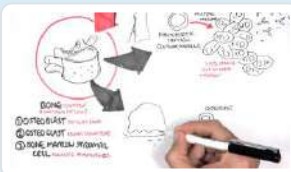
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Multiple Myeloma

CRASH! Medical Review - YouTube

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Multiple Myeloma

Armando Hasudungan - YouTube

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A 43-year-old man with acute pancreatitis is being treated in the surgical ward. Whilst an inpatient, he experiences recurrent epistaxis, gingival bleeding, and haematuria.

He is re-examined and multiple petechiae are noted as well as some mild confusion. He is somewhat hypotensive when observations are recorded.

Blood tests are taken:

Platelets	83 * 10 ⁹ /L	(150 - 400)
Prothrombin time (PT)	26 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	48 secs	(25-35 secs)
Fibrinogen	0.3 g/L	(2 - 4)

As well as general resuscitation, what else is most useful, first-line?

- ☐ Cryoprecipitate ×
- ☐ Fibrinogen concentrate ×
- ☐ Fresh frozen plasma ×
- ☐ Platelet transfusion ×
- ☐ Tranexamic acid ×

Submit answer

Reference ranges 

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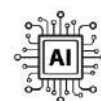
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Activated partial thromboplastin time (APTT)	48 secs	(25-35 secs)
Fibrinogen	0.3 g/L	(2 - 4)

As well as general resuscitation, what else is most useful, first-line?

Cryoprecipitate	30%
Fibrinogen concentrate	11%
Fresh frozen plasma	56%
Platelet transfusion	1%
Tranexamic acid	2%

In bleeding patients with DIC and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), administration of fresh frozen plasma (FFP) may be useful

Important for me Less important




This patient has developed disseminated intravascular coagulation (DIC), a syndrome characterised by coagulation pathway activation, leading to intravascular thrombi and depletion of platelets and coagulation factors. It is triggered by an underlying condition - in this scenario, acute pancreatitis. As well as treatment of the underlying disorder, the most useful additional option here is **fresh frozen plasma**. This is the preferred method of replacing coagulation factors when bleeding is present or when fibrinogen levels are low.

Cryoprecipitate is a second-line alternative. Fresh frozen plasma is still preferred with regards to DIC.

Similarly, **fibrinogen concentrate** may be used as second-line alternatives. However, fresh frozen plasma is the first-line choice for DIC.

Platelet transfusion is generally considered when the platelet count is less than $20 \times 10^9/L$, or less than $50 \times 10^9/L$ in the presence of active bleeding. In this scenario, therefore, this is not as important a consideration as the administration of fresh frozen plasma.

Tranexamic acid may be used in the management of chronic DIC, under specialist guidance. It should be used with extreme caution as it inhibits fibrinolytic pathways, which may worsen thrombosis. In the acute setting, such as this scenario, it does not play a role.

		 Discuss (4)	Improve
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Next question >

Disseminated intravascular coagulation ★

Under homeostatic conditions, coagulation and fibrinolysis are coupled. The activation of the coagulation cascade yields thrombin that converts fibrinogen to fibrin; the stable fibrin clot being the final product of hemostasis. The fibrinolytic system breaks down fibrinogen and fibrin. Activation of the fibrinolytic system generates plasmin (in the presence of thrombin), which is responsible for the lysis of fibrin clots. The breakdown of fibrinogen and fibrin results in polypeptides (fibrin degradation products). In a state of homeostasis, the presence of plasmin is critical, as it is the central proteolytic enzyme of coagulation and is also necessary for fibrinolysis.

In DIC, the processes of coagulation and fibrinolysis are dysregulated, and the result is widespread clotting with resultant bleeding. Regardless of the triggering event of DIC, once initiated, the pathophysiology of DIC is similar in all conditions. One critical mediator of DIC is the release of a transmembrane glycoprotein (tissue factor = TF). TF is present on the surface of many cell types (including endothelial cells, macrophages, and monocytes) and is not normally in contact with the general circulation, but is exposed to the circulation after vascular damage. For example, TF is released in response to exposure to cytokines (particularly interleukin 1), tumour necrosis factor, and endotoxin. This plays a major role in the development of DIC in septic conditions. TF is also abundant in tissues of the lungs, brain, and placenta. This helps to explain why DIC readily develops in patients with extensive trauma. Upon activation, TF binds with coagulation factors that then triggers the extrinsic pathway (via Factor VII) which subsequently triggers the intrinsic pathway (XII to XI to IX) of coagulation.

Causes of DIC

- sepsis
- trauma

- obstetric complications e.g. amniotic fluid embolism or hemolysis, elevated liver function tests, and low platelets (HELLP syndrome)
- malignancy

Diagnosis

A typical blood picture includes:

- ↓ platelets
- ↓ fibrinogen
- ↑ PT & APTT
- ↑ fibrinogen degradation products
- schistocytes due to microangiopathic haemolytic anaemia

Disorder	Prothrombin time	APTT	Bleeding time	Platelet count
Warfarin administration	Prolonged	Normal	Normal	Normal
Aspirin administration	Normal	Normal	Prolonged	Normal
Heparin	Often normal (may be prolonged)	Prolonged	Normal	Normal
DIC	Prolonged	Prolonged	Prolonged	Low



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Next question >

Textbooks

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Media



Disseminated intravascular coagulation

Osmosis - YouTube



2



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A 23-year-old man presents to the emergency department acutely unwell for the last 72 hours. He has been fatigued for the last month and has been having night sweats and has had several colds. Over the last 3 days, he has become more unwell, shivery and vomiting. He has noticed bruising on forearms and thighs. On examination, he is drowsy and has a temperature of 38.5°C. His blood pressure is 90/50 mmHg, heart rate 120/min. He is peripherally shut down with a cap refill time of 5 seconds. He has conjunctival pallor. He is given IV fluids and antibiotics by the emergency department. His blood results show:

Hb	89 g/l
Platelets	43 * 10 ⁹ /l
WBC	13.0 * 10 ⁹ /l
Neutrophils	9.0 * 10 ⁹ /l
D-Dimer	5.8mg/L (<0.5)
INR	8.5
PT	89 seconds (9-12)
APTT ratio	1.7 (0.8-1.2)
Fibrinogen	0.1g/L (1.5 - 4.5)
Blood film	Faggot cells seen

Na ⁺	138 mmol/l
K ⁺	5.8 mmol/l
Urea	18 mmol/l
Creatinine	195 µmol/l
CRP	170 mg/l

Bilirubin	8 µmol/l
ALP	102 u/l
ALT	300 u/l
Albumin	38 g/l

He is transferred to ITU for ionotropic support. He is treated with fresh frozen plasma which corrects his coagulopathy. Haematology is involved and he has a bone marrow analysis performed. Cytogenetics shows a translocation of chromosomes 15 and 17. What is the appropriate treatment to give?

<input type="radio"/>	All-trans retinoic acid	×
<input type="radio"/>	R-CHOP	×
<input type="radio"/>	Chlorambucil	×
<input type="radio"/>	High dose prednisolone	×
<input type="radio"/>	Ribavirin	×

Submit answer

Reference ranges ▾

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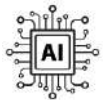
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All-trans retinoic acid	77%
R-CHOP	13%
Chlorambucil	5%
High dose prednisolone	4%
Ribavirin	1%



This patient has acute promyelocytic leukaemia (M3 subclass). This can present with DIC in young patients the prolonged prothrombin time, with platelets consumption and low fibrinogen. Faggot cells are hypergranular promyelocytes, so called because the high concentrations of Auer rods in the cytoplasm give the cells a bundle of sticks appearance. The gene translocation of 15:17 results in a fusion gene of PML:RARα (retinoic acid receptor). The exact process by which this gene fusion results in AML is unclear but the condition responds well to retinoic acid therapy hence this is the correct answer here. The other options are for other types of haematological malignancy.

Discuss (3)

Improve

Next question >

Acute promyelocytic leukaemia ★

You are not normally expected to be able to differentiate the different subtypes of acute myeloid leukaemia (AML) for the MRCP. An exception to this is acute promyelocytic leukaemia (APML, the M3 subtype of AML). The importance of identifying APML lies in both the presentation (classically disseminated intravascular coagulation) and management

APML is associated with the t(15;17) translocation which causes fusion of the PML and RAR-α genes.

Features

- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

APML is treated with all-trans retinoic acid (ATRA) to force immature granulocytes into maturation to resolve a blast crisis prior to more definitive chemotherapy.



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

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A 37-year-old woman was admitted to the Intensive Care Unit (ICU) two days following chemotherapy. She had received her third of six cycles of chemotherapy for malignant ovarian cancer and without initial complication and was discharged the same day. Two days later she felt unwell and developed a fever. After liaising with the oncology unit she was admitted directly to the Medical Admission Unit. A full septic screen was conducted and she was treated empirically for neutropaenic sepsis with intravenous tazocin and gentamicin. Other than malignant ovarian cancer her past medical history was unremarkable, and there was no known metastasis. She was not taking any other drug therapy and was a non smoker. She did not consume alcohol.

Unfortunately whilst on the Medical Admission Unit she continued to deteriorate, developing fluctuating hemiparesis of initially the left lower limb, and then the right upper limb. Her level of consciousness dropped and her speech had become slurred. An urgent transoesophageal echocardiogram and CT head scan was conducted, pending availability of a MRI scan. She was promptly transferred to the Intensive Care Unit.

Upon arrival at the ICU she appeared very unwell, with a GCS of 12/15. Her blood pressure was 188/96 mmHg, her heart rate was 112, her respiratory rate was 22/min and her temperature was 38.5 degrees celsius. Examination of the cardiovascular system revealed the presence of normal heart sounds, a JVP of 3cm and warm well perfused peripheries. Examination of the respiratory system revealed good air entry in both lungs, with an oxygen saturation of 95% on air. Examination of her gastrointestinal system was unremarkable. Examination of her neurological system revealed localization to pain stimulus, with confusion and eye opening only in response to verbal prompting. Her speech was slurred. There was no other apparent focal neurological deficit, with otherwise normal cranial nerve and peripheral nervous system testing.

The results of the investigations conducted are as follows:

Hb	89g/l
Platelets	$38 \times 10^9/l$
WBC	$15.2 \times 10^9/l$
Reticulocyte count	4% (ie above normal range)
Blood film	presence of schistocytes, normocytic normochromic anaemia

Na ⁺	136 mmol/l
K ⁺	6.1 mmol/l
Urea	10.1 mmol/l
Creatinine	154 μ mol/l

CRP	22 mg/l
ESR	45 mm/hr
Protein	78 g/l
Albumin	36 g/l
Adj calcium	2.42 mmol/l
Phosphate	0.95 mmol/l
Bilirubin	44 µmol/l
ALT	39 u/l
LDH	1286 u/l
ALP	102 u/l
PTT	14s
APTT	44s
INR	1.1
D-dimer	136 ng/ml

Chest x-ray: normal heart and lung appearances

ECG: heart rate 107bpm normal sinus rhythm, normal QRS and QTc intervals

Urinalysis: proteinuria ++, haematuria +, leuc/nit/glu negative

Blood MCS x3: pending result

Urine MCS: pending result

CT head: no space occupying lesion, mass shift or intracerebral haemorrhage seen

Transoesophageal echocardiogram: normal systolic function, normal appearance of all valves, no evidence of vegetation seen

In the context of the likely underlying diagnosis, what is the best immediate management step?

- ☐ Commence immediate plasma exchange ×
- ☐ Commence high dose intravenous hydrocortisone ×
- ☐ Commence platelet infusion ×
- ☐ Commence IV meropenem and IV antifungal therapy ×
- ☐ Commence fresh frozen plasma infusion ×

Submit answer

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CT head: no space occupying lesion, mass shift or intracerebral haemorrhage seen




Transoesophageal echocardiogram: normal systolic function, normal appearance of all valves, no evidence of vegetation seen

In the context of the likely underlying diagnosis, what is the best immediate management step?

Commence immediate plasma exchange	80%
Commence high dose intravenous hydrocortisone	4%
Commence platelet infusion	2%
Commence IV meropenem and IV antifungal therapy	6%
Commence fresh frozen plasma infusion	8%



This patient has developed thrombotic thrombocytopenia purpura (TTP) secondary to chemotherapy, as manifested by the combination haemolytic anaemia, thrombocytopenia and acute renal impairment. The presence of a fever and neurological involvement differentiates this condition from haemolytic-uraemic syndrome. Of the above options, plasma exchange holds the best prognosis for this condition and is, therefore, the best option to be initiated without delay, but in practice glucocorticoids and fresh frozen plasma infusions are often given pending arranging plasma exchange.

   Discuss (10) Improve

[Next question >](#)

Thrombotic thrombocytopenic purpura: management ★







Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of protease which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management

- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine

[Next question >](#)

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Textbooks

High-yield textbook

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Links

British Journal of Haematology

 4  4

[2012 TTP guidelines](#)

[Suggest link](#)

[Report broken link](#)

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A 22-year-old man with sickle cell disease is seen in the Emergency Department. He has had worsening pain in his arms and legs for the last 2 days and 5 hours ago developed a painful sustained erection.

He has felt otherwise well recently and has no other past medical history. He is on regular paracetamol, ibuprofen, folate and penicillin. He does not receive regular transfusions and has been admitted with a crisis only once before. He has never had an episode of painful sustained erection.

On examination he has a heart rate of 110 beats per minute and a blood pressure of 132/95 mmHg. His oxygen saturations are 96% on room air and he is afebrile. His chest is clear and abdomen is soft. He has no swelling or erythema of his limbs, though they are generally tender. He continues to have an erection, though there is no sign of ischaemia.

His chest x-ray shows clear lung fields.

His blood tests are as follows:

Hb	78 g/l	Na ⁺	141 mmol/l
Platelets	331 * 10 ⁹ /l	K ⁺	3.7 mmol/l
WBC	9 * 10 ⁹ /l	Urea	5 mmol/l
Neuts	7 * 10 ⁹ /l	Creatinine	86 µmol/l
Lymphs	1.6 * 10 ⁹ /l	CRP	14 mg/l

He is treated with intravenous fluids and generous analgesia with diamorphine. His limb pain is improved but he continues to have a painful erection.

What is the next most appropriate step?

- ☐ Adrenalin ×
- ☐ Diethylstilbestrol ×
- ☐ Exchange transfusion ×
- ☐ Review by urologist ×
- ☐ Sildenafil ×

Submit answer

Reference ranges ▾

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A 22-year-old man with sickle cell disease is seen in the Emergency Department. He has had worsening pain in his arms and legs for the last 2 days and 5 hours ago developed a painful sustained erection.

He has felt otherwise well recently and has no other past medical history. He is on regular paracetamol, ibuprofen, folate and penicillin. He does not receive regular transfusions and has been admitted with a crisis only once before. He has never had an episode of painful sustained erection.

On examination he has a heart rate of 110 beats per minute and a blood pressure of 132/95 mmHg. His oxygen saturations are 96% on room air and he is afebrile. His chest is clear and abdomen is soft. He has no swelling or erythema of his limbs, though they are generally tender. He continues to have an erection, though there is no sign of ischaemia.

His chest x-ray shows clear lung fields.

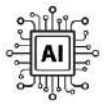
His blood tests are as follows:

Hb	78 g/l	Na ⁺	141 mmol/l
Platelets	331 * 10 ⁹ /l	K ⁺	3.7 mmol/l
WBC	9 * 10 ⁹ /l	Urea	5 mmol/l
Neuts	7 * 10 ⁹ /l	Creatinine	86 µmol/l
Lymphs	1.6 * 10 ⁹ /l	CRP	14 mg/l

He is treated with intravenous fluids and generous analgesia with diamorphine. His limb pain is improved but he continues to have a painful erection.

What is the next most appropriate step?

Adrenalin	3%
Diethylstilbestrol	10%
Exchange transfusion	60%
Review by urologist	23%
Sildenafil	4%



This gentleman has priapism, a sustained painful erection lasting 4 hours. If left untreated it can result in impotence. Current guidelines recommend initial conservative management with fluids and analgesia. Although any interventions beyond this have variable results, evidence supports prompt urology review to determine the need for surgical management including drainage. There is insufficient evidence to recommend routine exchange transfusions. Sildenafil, diethylstilbestrol and adrenalin may be used in consultation with urology but evidence of benefit is variable.

Reference - NIH Evidence-based management of sickle cell disease expert panel report 2014

		Discuss (8)	Improve
--	--	-------------	---------

Next question >

Sickle-cell crises ★

Sickle cell anaemia is characterised by periods of good health with intervening crises

A number of types of crises are recognised:

- thrombotic, 'vaso-occlusive', 'painful crises'
- acute chest syndrome
- anaemic
 - aplastic
 - sequestration
- infection

Thrombotic crises

- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation (e.g. high altitude)
- painful vaso-occlusive crises should be diagnosed clinically - there isn't one test that can confirm them although tests may be done to exclude other complications
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain)

Acute chest syndrome

- vaso-occlusion within the pulmonary microvasculature → infarction in the lung parenchyma
- dyspnoea, chest pain, pulmonary infiltrates on chest x-ray, low pO₂
- management
 - pain relief
 - respiratory support e.g. oxygen therapy

- antibiotics: infection may precipitate acute chest syndrome and the clinical findings (respiratory symptoms with pulmonary infiltrates) can be difficult to distinguish from pneumonia
- transfusion: improves oxygenation
- the most common cause of death after childhood

Aplastic crises

- caused by infection with parvovirus
- sudden fall in haemoglobin
- bone marrow suppression causes a reduced reticulocyte count

Sequestration crises

- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- associated with an increased reticulocyte count



123



Next question >

B

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Textbooks

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Links

British Society for Haematology



6



13

[2015 Management of acute chest syndrome in sickle cell disease](#)

Clinical Knowledge Summaries



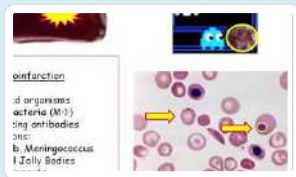
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7

[Sickle Cell Disease guidelines](#)

Media





Sickle cell anaemia

12DaysinMarch - YouTube  2  0





Sickle cell anaemia

AK lectures - YouTube  1  0













Sickle cell anaemia

Osmosis - YouTube  1  2

Report broken media

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A 23 year old male of Nigerian descent is referred from the ED with acute shortness of breath associated with fever and dry cough. His shortness of breath has limited him to an exercise tolerance of around 10 yards. He also complains of excruciating right sided chest pain. He is known to have sickle cell anaemia and has had no admissions to the hospital in the last 3 years.

Observations

- heart rate 94bpm regular
- blood pressure 112/74 mmHg
- temperature 38.3
- respiratory rate 22
- urine output under 30ml/hr
- oxygen saturations 93% on room air

Examination

- respiratory system shallow breathing, bronchial breath sounds with crepitations to right base

Blood results:

Hb	7.7 g/dl
Platelets	200 * 10 ⁹ /l
WBC	13.2 * 10 ⁹ /l

Bilirubin	36 µmol/l
Urea	8.2 mmol/l
Creatinine	146 µmol/l

What is the most important initial steps in management?

- ☐ Oxygen, IV fluids, antibiotics and analgesia ×
- ☐ 2 unit blood transfusion and analgesia ×
- ☐ Oxygen and analgesia only ×

☐ Antibiotics and IV fluid only ✕

☐ Plasmapheresis and analgesia ✕

Submit answer

Reference ranges ▾

Score: **0%**

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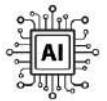
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WBC	13.2 * 10 ⁹ /l

Bilirubin	36 µmol/l
Urea	8.2 mmol/l
Creatinine	146 µmol/l

What is the most important initial steps in management?

Oxygen, IV fluids, antibiotics and analgesia	76%
2 unit blood transfusion and analgesia	4%
Oxygen and analgesia only	7%



It is important to recognise and treat sickle cell crises (as detailed above) as a matter of urgency. This condition can be quickly fatal. This patient should be treated as per sepsis guidelines. It is crucial to adequately control the pain in this patient cohort as not being able to inhale deeply due to pain will only serve to worsen the lung damage. Early assessment for the involvement of the critical care team is required as acute respiratory distress syndrome is a real possibility. Oxygen saturation levels should be maintained above 95% in a patient where a normal steady state level is not known. Management of this and the haemoglobin level should be specific for the patient and compared to past levels. The question states that the patient has had no admissions to the hospital in the last 3 years and as such the aim should be to keep oxygen saturations above 95%.



Discuss (9)

Improve

[Next question >](#)

Sickle-cell crises ★

Sickle cell anaemia is characterised by periods of good health with intervening crises

A number of types of crises are recognised:

- thrombotic, 'vaso-occlusive', 'painful crises'
- acute chest syndrome
- anaemic
 - aplastic
 - sequestration
- infection

Thrombotic crises

- also known as painful crises or vaso-occlusive crises
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Aplastic crises

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- sudden fall in haemoglobin
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Sequestration crises

- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
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123



Next question >

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Links

British Society for Haematology

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2015 Management of acute chest syndrome in sickle cell disease

Clinical Knowledge Summaries

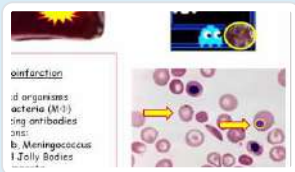
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Sickle Cell Disease guidelines

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Media



[Sickle cell anaemia](#)

12DaysinMarch - YouTube 👍 2 👎 0



[Sickle cell anaemia](#)

AK lectures - YouTube 👍 1 👎 0



[Sickle cell anaemia](#)

Osmosis - YouTube 👍 1 👎 2

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Question 29 of 191



A 64-year-old female undergoing chemotherapy treatment with mitomycin for bladder cancer presents to the Emergency Department with confusion, epistaxis and a widespread rash. On examination, she is febrile and has a diffuse petechial rash.

Hb	10.6g/dl
Platelets	54 * 10 ⁹ /l
WBC	11.2 * 10 ⁹ /l
Urea	11mmol/l
Creatinine	117µmol/l
Bilirubin	58µmol/l
ALP	42u/l

A blood film shows fragmented erythrocytes.

What is the most appropriate treatment for this patient?

- ☐ Renal dialysis ×
- ☐ Supportive treatment ×
- ☐ A pool of platelets and fluid resuscitation ×
- ☐ Urgent plasma exchange ×
- ☐ IV tazocin, a pool of platelets and fluid resuscitation ×

Submit answer

Reference ranges 

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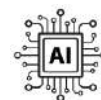
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WBC	11.2 * 10 ⁹ /l
Urea	11mmol/l
Creatinine	117µmol/l
Bilirubin	58µmol/l
ALP	42u/l

A blood film shows fragmented erythrocytes.

What is the most appropriate treatment for this patient?

Renal dialysis	1%
Supportive treatment	14%
A pool of platelets and fluid resuscitation	5%
Urgent plasma exchange	71%
IV tazocin, a pool of platelets and fluid resuscitation	9%



Thrombotic thrombocytopenic purpura (TTP) is characterised by fluctuating neurological signs, fever, renal dysfunction, microangiopathic haemolysis and thrombocytopenia. The key to diagnosis is differentiating between TTP and haemolytic-uraemic syndrome (HUS). The presence of neurological signs in TTP and more severe renal dysfunction in HUS usually helps in distinguishing the two.

Congenital TTP is caused by a deficiency in von Willebrand factor. However, the majority of cases are secondary and can occur in pregnancy, HIV and associated with some drugs. In particular, the chemotherapeutic agents mitomycin C, bleomycin, tamoxifen and gemcitabine are all associated with secondary TTP. Other drugs in association include penicillin, rifampicin and

immunosuppressive drugs eg. ciclosporin A.

The standard treatment for TTP is IV plasma exchange which should be initiated as soon as possible.





 Discuss (5)

Improve

Next question >

Thrombotic thrombocytopenic purpura: management ★

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)






- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of protease which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management

- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine



Next question >

B *I*  **A** ▼    ▼ **T** ▼  ▼  

Textbooks

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Links

British Journal of Haematology

 4  4

[2012 TTP guidelines](#)

[Suggest link](#)

[Report broken link](#)

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A 22-year-old man attends the emergency department with a group of friends from a university party. He complains of worsening shortness of breath and light-headedness. He appears panicked and is clutching his chest. There is no past medical history of note and he has no allergies.

His observations are as follows:






- Temperature 36.2°C
- Heart rate 112 beats/min
- Blood pressure 120/75mmHg
- Respiratory rate 24 breaths/min
- Oxygen saturations 90% on air

On examination, his lips are cyanosed. His chest is clear with good air entry bilaterally and his heart sounds are normal. Peripheral pulses are present with a capillary refill of <2 seconds and his calves are soft and non-tender.

Arterial blood gas:

pH	7.21	(7.35 - 7.45)
pO ₂	12.1 kPa	(11 - 14.4)
pCO ₂	2.4 kPa	(4.6 - 6.4)
Bicarbonate	16 mmol/L	(22 - 29)
Chloride	100 mmol/L	(95 - 108)
Lactate	1.2 mmol/L	(0.5 - 2.2)
Glucose	5.6 mmol/L	(4 - 7)

Given the likely diagnosis, which of the following is the most appropriate next step in the management of this patient?

- ☐ Fomepizole 
- ☐ Hyperbaric oxygen 
- ☐ Methylene blue 
- ☐ Thrombolysis 
- ☐ Intravenous 1.26% sodium bicarbonate 

Submit answer

Reference ranges ▾

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Lactate	1.2 mmol/L	(0.5 - 2.2)
Glucose	5.6 mmol/L	(4 - 7)

Given the likely diagnosis, which of the following is the most appropriate next step in the management of this patient?

Fomepizole

7%

Hyperbaric oxygen

6%

Methylene blue

82%

Thrombolysis

1%

Intravenous 1.26% sodium bicarbonate

5%

Methylene blue can be used to treat methaemoglobinaemia. It causes a reduction of Fe^{3+} (ferric) to Fe^{2+} (ferrous)

Important for me Less important



This patient has methaemoglobinaemia, likely secondary to drug misuse (e.g. amyl nitrite poppers) at a party. In patients with methaemoglobinaemia, haemoglobin has been oxidised from Fe^{2+} to Fe^{3+} . This oxidised form of haemoglobin cannot bind to oxygen and therefore symptoms include cyanosis, shortness of breath and headache. In more severe illnesses, investigations may detect metabolic acidosis and arrhythmias. During methaemoglobinaemia, a normal PO_2 may be seen with reduced oxygen saturations, similar to this patient. The treatment of choice for methaemoglobinaemia is intravenous methylene blue, which causes a reduction reaction to convert Fe^{3+} back to Fe^{2+} .

Fomepizole is used in the treatment of ethanol toxicity. Symptoms of ethanol toxicity are initially similar to alcohol excess with confusion, slurred speech and altered gait. Metabolic acidosis and acute kidney injury follow. However, ethanol toxicity does not explain this patient's hypoxia and cyanosis and is less likely to be correct.

Hyperbaric oxygen therapy is used in the treatment of carbon monoxide poisoning. Unlike methaemoglobinaemia, symptoms of carbon monoxide poisoning include headache, confusion and nausea and vomiting. Respiratory symptoms are less predominant compared to methaemoglobinaemia. Carbon monoxide poisoning tends to produce a normal oxygen saturation level with a low PO_2 , unlike this patient. It also does not explain this patient's metabolic acidosis and suggests an alternative diagnosis.

Thrombolysis would be an option for the treatment of a thrombotic cause of this patient's symptoms (e.g. pulmonary embolism). However, patients with a pulmonary embolism are more likely to have a metabolic alkalosis secondary to hyperventilation, in contrast to this patient with metabolic acidosis.

Sodium bicarbonate can be used to treat severe metabolic acidosis. However, it is not used first-line in the treatment of methaemoglobinaemia and the priority should be to reverse the oxidation process of haemoglobin.



Discuss (2)

Improve

Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO_2 but decreased oxygen saturation

Management

- NADH methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



123



Next question >

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Textbooks

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Extended textbook



Links

Life in the Fast Lane

 6  3

[Methaemoglobinaemia](#)

The Internet Book of Critical Care

 10  4

[Methemoglobinemia](#)



[Suggest link](#)

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Media



[Methaemoglobinaemia](#)

Osmosis - YouTube  7  2

[Report broken media](#)

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A 33-year-old patient presents to the emergency department feeling very lethargic and tired over the last week. He has been increasingly short of breath on exertion and his exercise tolerance has fallen to a few hundred yards before he is out of breath. He is a known sickle cell disease patient who is managed by the Haematology team in your hospital. On examination he is afebrile and heart rate and blood pressure are within normal limits. His respiratory rate is 16/min and his oxygen saturation is 98% on air. He does become noticeably short of breath on minimal movement.

His blood tests show:

Hb	65 g/l
Platelets	$46 \times 10^9/l$
WBC	$2.5 \times 10^9/l$
Neuts	$1.2 \times 10^9/l$
Haptoglobins	1.9 g/L (0.3-2.0)
Reticulocytes	$8.9 \times 10^9/L$ (25-80)

Na ⁺	136 mmol/l
K ⁺	3.9 mmol/l
Urea	7.4 mmol/l
Creatinine	78 μ mol/l
CRP	<3 mg/L (<10)
LDH	200 IU/L (200-500)

Bilirubin	4 μ mol/l
ALP	89 u/l
ALT	34 u/l
Albumin	39 g/l

His chest x-ray is normal.

On further questioning, he tells you that his 5-year-old daughter was unwell 3 weeks ago. He took her to see the GP and was told it was likely to be a viral illness. What is the most likely cause for his blood results as shown?

<input type="radio"/>	Parvovirus B19	×
<input type="radio"/>	Acute chest crisis	×
<input type="radio"/>	Splenic sequestration	×
<input type="radio"/>	HIV	×
<input type="radio"/>	Legionella pneumoniae	×

Submit answer

Reference ranges ▾

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A 33-year-old patient presents to the emergency department feeling very lethargic and tired over the last week. He has been increasingly short of breath on exertion and his exercise tolerance has fallen to a few hundred yards before he is out of breath. He is a known sickle cell disease patient who is managed by the Haematology team in your hospital. On examination he is afebrile and heart rate and blood pressure are within normal limits. His respiratory rate is 16/min and his oxygen saturation is 98% on air. He does become noticeably short of breath on minimal movement.

His blood tests show:

Hb	65 g/l
Platelets	46 * 10 ⁹ /l
WBC	2.5 * 10 ⁹ /l
Neuts	1.2 * 10 ⁹ /l
Haptoglobins	1.9 g/L (0.3-2.0)
Reticulocytes	8.9 x10 ⁹ /L (25-80)

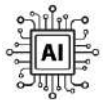
Na ⁺	136 mmol/l
K ⁺	3.9 mmol/l
Urea	7.4 mmol/l
Creatinine	78 µmol/l
CRP	<3 mg/L(<10)
LDH	200 IU/L (200-500)

Bilirubin	4 µmol/l
ALP	89 u/l
ALT	34 u/l
Albumin	39 g/l

His chest x-ray is normal.

On further questioning, he tells you that his 5-year-old daughter was unwell 3 weeks ago. He took her to see the GP and was told it was likely to be a viral illness. What is the most likely cause for his blood results as shown?

Parvovirus B19	94%
Acute chest crisis	2%
Splenic sequestration	3%
HIV	0%
Legionella pneumoniae	0%



This gentleman has had an aplastic sickle cell crisis as a result of parvovirus infection. He has symptomatic anaemia. There is nothing to suggest splenic sequestration and he is too well for an acute chest syndrome. The normal chest x-ray is not in keeping with a pneumonia. HIV is a possibility but less likely given the clinical picture.

Discuss (6)

Improve

Next question >

Sickle-cell crises ★

Sickle cell anaemia is characterised by periods of good health with intervening crises

A number of types of crises are recognised:

- thrombotic, 'vaso-occlusive', 'painful crises'
- acute chest syndrome
- anaemic
 - aplastic
 - sequestration
- infection

Thrombotic crises

- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation (e.g. high altitude)
- painful vaso-occlusive crises should be diagnosed clinically - there isn't one test that can confirm them although tests may be done to exclude other complications
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain)

Acute chest syndrome

- vaso-occlusion within the pulmonary microvasculature → infarction in the lung parenchyma
- dyspnoea, chest pain, pulmonary infiltrates on chest x-ray, low pO₂
- management
 - pain relief
 - respiratory support e.g. oxygen therapy
 - antibiotics: infection may precipitate acute chest syndrome and the clinical findings (respiratory symptoms with pulmonary infiltrates) can be difficult to distinguish from pneumonia
 - transfusion: improves oxygenation
- the most common cause of death after childhood

Aplastic crises

- caused by infection with parvovirus
- sudden fall in haemoglobin
- bone marrow suppression causes a reduced reticulocyte count

Sequestration crises

- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- associated with an increased reticulocyte count



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Next question >

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Textbooks

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Links

British Society for Haematology

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2015 Management of acute chest syndrome in sickle cell disease

Clinical Knowledge Summaries

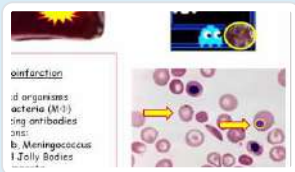
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Sickle Cell Disease guidelines

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Media



[Sickle cell anaemia](#)

12DaysinMarch - YouTube 👍 2 👎 0



[Sickle cell anaemia](#)

AK lectures - YouTube 👍 1 👎 0



[Sickle cell anaemia](#)

Osmosis - YouTube 👍 1 👎 2

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A 79-year-old woman has been referred to the clinic due to weight loss, right-sided chest pain, lower back pain, and general fatigue.

Hb	96 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$399 \times 10^9/\text{L}$	(150 - 400)
WBC	$10.2 \times 10^9/\text{L}$	(4.0 - 11.0)
Na ⁺	145 mmol/L	(135 - 145)
K ⁺	4.5 mmol/L	(3.5 - 5.0)
Urea	15.2 mmol/L	(2.0 - 7.0)
Creatinine	190 $\mu\text{mol}/\text{L}$	(55 - 120)
Calcium	3.1 mmol/L	(2.1-2.6)
Phosphate	1.4 mmol/L	(0.8-1.4)
Magnesium	0.7 mmol/L	(0.7-1.0)

Urine Bence Jones: positive

She is usually fit and well with no past medical history.

What would be the first-line imaging to confirm the most likely diagnosis?

- ☐ CT thorax, abdomen, and pelvis
- ☐ Chest radiograph
- ☐ PET CT
- ☐ Skeletal survey
- ☐ Whole-body MRI

Submit answer

Reference ranges

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Urine Bence Jones: positive

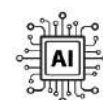
She is usually fit and well with no past medical history.

What would be the first-line imaging to confirm the most likely diagnosis?

CT thorax, abdomen, and pelvis	2%
Chest radiograph	1%
PET CT	5%
Skeletal survey	20%
Whole-body MRI	73%

Whole body MRI 1st line imaging in suspected multiple myeloma

Important for me Less important



The most likely diagnosis here is multiple myeloma given the weight loss, bone pain, anaemia, renal impairment, and hypercalcaemia.

Further tests should be sent to clarify this diagnosis including serum free light chains, serum protein electrophoresis, and immunoglobulins.

It is worth noting that guidance regarding the answer to this question may vary from hospital to hospital depending on availability, but national guidance recommends whole-body MRI as first-line imaging.


Whole-body MRI is the correct answer. Part of the diagnostic criteria for multiple myeloma is the presence of 1 or more osteolytic lesions of ≥ 5 mm. This is most sensitively picked up on MRI scanning, which can also pick up pre-lytic lesions that may be amenable to biopsy.

CT thorax, abdomen, and pelvis is incorrect. CT scanning has a lower sensitivity for osteolytic lesions. There is also higher radiation exposure.

PET CT is incorrect. This type of scanning can be helpful for looking at intramedullary involvement, but the consensus from current best evidence is that MRI is preferable particularly to identify osteolytic lesions.

Skeletal survey is incorrect. It is less sensitive and specific compared to PET CT and MRI scanning. This is the preferred option for patients who are unable to undergo whole-body MRI, PET CT, or CT. It takes less time to perform compared to whole-body MRI (25 minutes as opposed to 60 minutes).

Chest radiograph is incorrect. Although this is a sensible first-line test to perform in the acute setting, this question asks specifically about the first-line test for the most likely diagnosis here - multiple myeloma. Chest radiograph is therefore incorrect.

		 Discuss	Improve
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Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
 - much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
 - this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



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Next question >

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

Textbooks

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Links

Clinical Knowledge Summaries

 10  10

[Haematological cancers - recognition and referral](#)

NICE

 12  6

[2016 myeloma guidelines](#)

[Suggest link](#)



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Media



[Multiple Myeloma - Diagnosis and Treatment](#)

Medicosis Perfectionalis - YouTube

 6  0



[Multiple Myeloma](#)



Medicosis Perfectionalis - YouTube

 4  0



[Multiple Myeloma Mnemonic...the story of the plasma cell](#)

Medicosis Perfectionalis - YouTube

 5  1



What is multiple myeloma?

Khan Academy - YouTube

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Multiple Myeloma

Townsend Teaching - YouTube

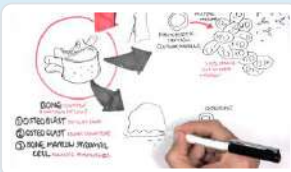
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Multiple Myeloma

CRASH! Medical Review - YouTube

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Multiple Myeloma

Armando Hasudungan - YouTube

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A 23-year-old female has presented with her first episode of seizure on the labour ward, 2 days after delivering her first child by normal vaginal delivery. She reports a fluctuating generalised headache over the past 3 months but had not previously sought medical attention. In addition, she had spiked 2 fevers over 38°C over the past 48 hours, with no dysuria, diarrhoea or vomiting, productive cough or signs of meningism. She has no past medical history, is a life-long non-smoker and has been abstinent from alcohol for 9 months, previously drinking 4 units per week. Her seizure was witnessed and described as tonic-clonic jerking of all 4 limbs, associated with loss of consciousness, terminated after 4mg of intravenous lorazepam after 4 minutes. On examination, she appears post-ictal but responding to voice despite being sleepy. Pupils are reactive and equal. Plantars are downgoing bilaterally. Cardiovascular, abdominal and respiratory examinations are unremarkable. No skin rashes, neck stiffness or photophobia are noted. Her blood results are as follows:

Hb	75 g/l
MCV	87 fl
Platelets	23 * 10 ⁹ /l
WBC	9.2 * 10 ⁹ /l
Blood film	schistocytes
Coombs' test	negative
CRP	30 mg/l
Urea	12.6mmol/l
Creatinine	154 µmol/l
Bilirubin	28 µmol/l
ALP	98 u/l
ALT	28 u/l
γGT	23 u/l

A CT head with contrast demonstrated no areas of ischaemia, haemorrhage or space occupying lesion.

Which is the next most appropriate immediate management?

- ☐ Plasma exchange ×
- ☐ Intravenous 3rd generation cephalosporin antibiotics ×

- | | |
|---|---|
| <input type="radio"/> Intravenous phenytoin loading | × |
| <input type="radio"/> MRI head with contrast | × |
| <input type="radio"/> Intravenous steroids | × |

Submit answer

Reference ranges ▾

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ALP	98 u/l
ALT	28 u/l
γGT	23 u/l

A CT head with contrast demonstrated no areas of ischaemia, haemorrhage or space occupying lesion.

Which is the next most appropriate immediate management?

Plasma exchange	84%
Intravenous 3rd generation cephalosporin antibiotics	3%

Intravenous phenytoin loading

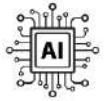
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MRI head with contrast

3%

Intravenous steroids

8%



This young lady's blood tests demonstrated a normocytic anaemia associated with schistocytes (fragmented red cells) with negative Coombs' test, suggestive of mechanical destruction of red cells. In addition, thrombocytopaenia is present with renal impairment and normal liver function tests. The initial presentation is of first seizure and fluctuating headache, with two unexplained fevers. The pentad of fever, fluctuating neurological symptoms, microangiopathic haemolytic anaemia, thrombocytopaenia and renal impairment represents thrombotic thrombocytopaenic purpura-haemolytic uraemic syndrome spectrum (TTP-HUS), resulting in microvascular thrombus formation. There is little to suggest an underlying epilepsy syndrome and no indication for phenytoin loading after a single seizure without status epilepticus. While meningitis may cause headaches, a fluctuating 3-month history without meningism is unlikely.

Immediate treatment of TTP-HUS is reliant on plasma exchange without delay in order to remove the high-molecular weight von-Willebrand factor (vWF) driving platelet aggregation and replacing ADAMTS-13 protease, a cleavage enzyme of high molecular weight vWF often deficient in TTP patients, resulting in microvascular thrombi formation. High dose steroids may be appropriate in the setting of refractory disease despite plasma exchange but is an adjunct to plasma exchange, not in place of. Persistent recurrent or refractory TTP-HUS despite plasma exchange and steroids should be considered for the addition of rituximab or increased frequency of plasma exchange. TTP-HUS is a medical emergency and invariably results in death secondary to progressive renal failure if not treated immediately.



Discuss (5)

Improve

Next question >

Thrombotic thrombocytopenic purpura: management ★

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of protease which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management


- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine

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Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

British Journal of Haematology

2012 TTP guidelines

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[Suggest link](#) [Report broken link](#)

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A 22-year-old man presents to the emergency department with shortness of breath. He takes no regular medicines and denies the use of herbal, or over-the-counter medications. However, he does admit to using amyl nitrites recreationally.

Observations are as follows: heart rate 125 beats per minute, respiratory rate 24 breaths per minute, blood pressure 125/75 mmHg, temperature 37.2 °C, and SpO₂ 92%. His chest is clear on auscultation.

He is started on 15L O₂ via a non-rebreather mask.

Blood gas analysis results are as follows:

pH	7.26	(7.35 - 7.45)
PaO ₂	72.4 kPa	(10.3 - 13.3 kPa)
PaCO ₂	2.9 kPa	(4.7 - 6 kPa)
HCO ₃	18 mmol/L	(22 - 28 mmol/L)
SaO ₂	48%	(94 - 98%)
Lactate	3.2 mmol/L	(<1.0)

What treatment is indicated?

- ☐ Ascorbic acid ×
- ☐ Dicobalt edetate ×
- ☐ Hydroxocobalamin ×
- ☐ Hyperbaric oxygen ×
- ☐ Methylthioninium chloride ×

Submit answer

Reference ranges ∨

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Blood gas analysis results are as follows:

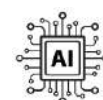
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HCO ₃	18 mmol/L	(22 - 28 mmol/L)
SaO ₂	48%	(94 - 98%)
Lactate	3.2 mmol/L	(<1.0)

What treatment is indicated?

Ascorbic acid	21%
Dicobalt edetate	4%
Hydroxocobalamin	8%
Hyperbaric oxygen	5%
Methylthioninium chloride	63%

Methylene blue can be used to treat methaemoglobinaemia. It causes a reduction of Fe³⁺ (ferric) to Fe²⁺ (ferrous)

Important for me Less important



The striking feature, in this case, is the significant discrepancy between the PaO₂ and SaO₂ on arterial blood gas analysis.

Given the patient is on 15L O₂, the PaO₂ is at a level expected indicating that gas exchange at the level of the alveoli is not impaired. There are various formulas for predicting the expected PaO₂ for any given inspired O₂ concentration. The Advanced Life Support (ALS) guidelines suggest that the PaO₂ for any given inspired concentration should be approximately 10 less than the inspired concentration (%). For example, in this case, 15L O₂ is equivalent to approximately 80-85% so we would expect the PaO₂ to be around 70 kPa.

However, it is important to note that the SaO₂ (oxygen saturation of haemoglobin) is markedly low at 48% indicating impaired oxygen binding to haemoglobin. It is also important to note that the peripheral SpO₂ is 92% which is clearly discrepant with the SaO₂. The two main causes of this picture are methaemoglobinaemia and carboxyhaemoglobinaemia. Because standard pulse oximeters are not capable of differentiating between different forms of bound haemoglobin, the SpO₂ is usually falsely high in these conditions.

Tissue hypoxia can be a consequence of 4 main causes:

- 1. Hypoxaemia (low PaO₂ due to poor gas exchange at the alveoli)
- 2. Toxic haemoglobin (low SaO₂ due to methaemoglobinaemia or carboxyhaemoglobinaemia)
- 3. Perfusional (e.g. shock, or localised causes such as compartment syndrome or bowel ischaemia)
- 4. Severe anaemia

Regardless of the cause, tissue hypoxia will result in lactic acidosis. Therefore, in patients with lactic acidosis, all the aforementioned causes should be considered. The patient in this case most certainly has lactic acidosis as a consequence of toxic haemoglobin-induced tissue hypoxia. He is acidotic with low serum bicarbonate since this acts as a buffer for lactic acid.

Methylthioninium chloride is correct. The patient has a diagnosis of acquired methaemoglobinaemia. As discussed above, the biochemical results are suggestive of toxic haemoglobin. The history of nitrate exposure favours the diagnosis of acquired methaemoglobinaemia. The treatment of choice is IV methylthioninium chloride (methylene blue).

Ascorbic acid is incorrect. This drug can be used to treat congenital methaemoglobinaemia. Although this remains within the differential diagnosis, the absence of previous episodes and the presence of a known risk factor (e.g. nitrate exposure) favours the acquired form.

Dicobalt edetate and **Hydroxocobalamin** are incorrect. These drugs can be used to treat cyanide poisoning. Cyanide binds the ferric (Fe³⁺) ion of cytochrome oxidase causing 'histotoxic hypoxia' and lactic acidosis. It would not cause a marked reduction of SaO₂ as seen in this case unless it was associated with coexistent carbon monoxide poisoning (e.g. due to smoke inhalation). There is nothing in this clinical case to suggest that this is the case.

Hyperbaric oxygen is incorrect. This can be used to treat severe carboxyhaemoglobinaemia.

Although carbon monoxide poisoning presents similarly and remains within the differential diagnosis, the history of nitrate exposure favours the diagnosis of methaemoglobinaemia.



Discuss (3)

Improve

Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO_2 but decreased oxygen saturation

Management

- NADH methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



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123



Next question >

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Textbooks

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Links

Life in the Fast Lane

 6  3

[Methaemoglobinaemia](#)

The Internet Book of Critical Care

 10  4

[Methemoglobinemia](#)



[Suggest link](#)

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Media





[Methaemoglobinaemia](#)


Osmosis - YouTube  7  2


[Report broken media](#)

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A 31-year-old lady presents to the emergency department with abdominal pain.

Her medical and surgical history is unremarkable other than mild depression and hay fever. Medications include paroxetine and PRN loratadine.

She complains of generalised colicky abdominal pain and has vomited once in the department.

On examination blood pressure is 155/86mmHg, heart rate is 95bpm and temperature is 37.9°C. Digital rectal examination reveals hard stool in the rectum.

Investigations reveal:

Hb	131 g/l
Platelets	362 * 10 ⁹ /l
WBC	7.3 * 10 ⁹ /l
Na ⁺	121 mmol/l
K ⁺	3.3 mmol/l
Urea	6.2 mmol/l
Creatinine	87 µmol/l
Urine dipstick	protein ++, leucocytes ++

What is the most likely diagnosis?

- ☐ Cholecystitis ×
- ☐ Acute porphyria ×
- ☐ Intestinal obstruction ×
- ☐ Pyelonephritis ×
- ☐ Systemic lupus erythematosus ×

Submit answer

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Question 35 of 191



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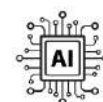
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Urea	6.2 mmol/l
Creatinine	87 µmol/l
Urine dipstick	protein ++, leucocytes ++

What is the most likely diagnosis?

Cholecystitis	1%
Acute porphyria	79%
Intestinal obstruction	8%
Pyelonephritis	8%
Systemic lupus erythematosus	3%



The normal white cell count make infective diagnoses such as pyelonephritis and cholecystitis less likely. Intestinal obstruction usually presents with an empty rectum.

The history of neuropsychiatric symptoms along with hypertension and hyponatraemia are suggestive of acute porphyria.

Systemic lupus erythematosus doesn't tend to present with abdominal pain.

		 Discuss (12)	Improve
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Next question >

Acute intermittent porphyria ★

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40-year-olds. AIP is more common in females (5:1)

The classical presentation is a combination of abdominal, neurological and psychiatric symptoms:

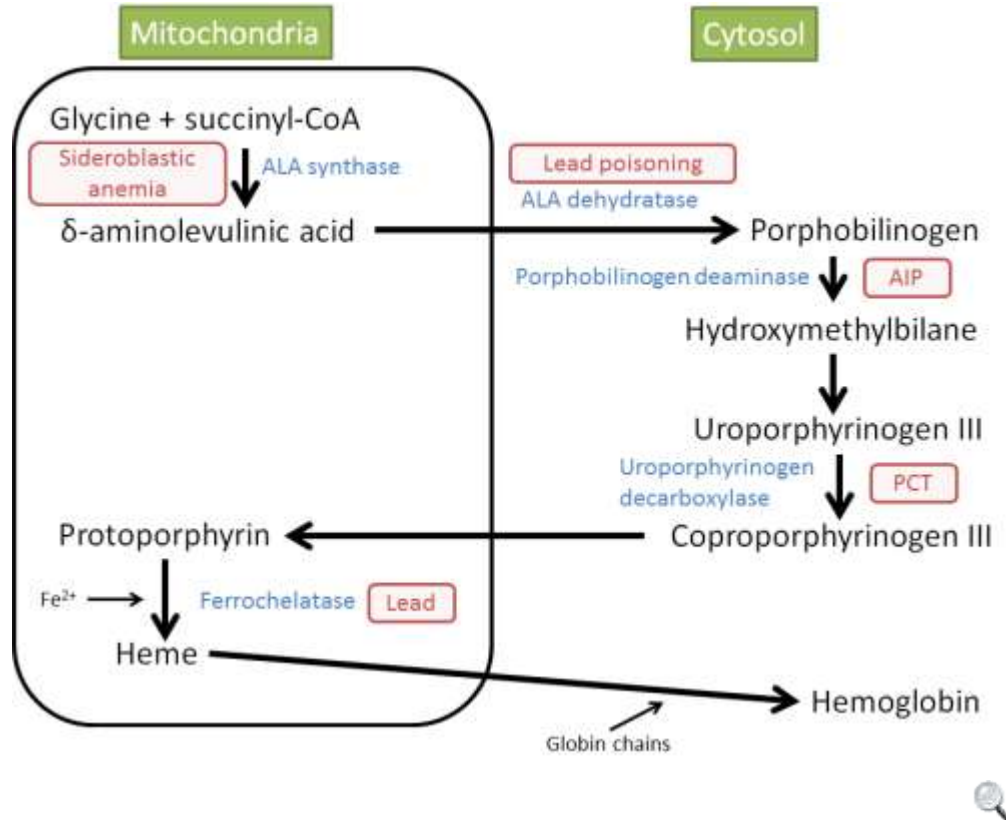
- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

Diagnosis

- classically urine turns deep red on standing
- raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
- assay of red cells for porphobilinogen deaminase
- raised serum levels of delta aminolaevulinic acid and porphobilinogen

Management

- avoiding triggers
- acute attacks
 - IV haematin/haem arginate
 - IV glucose should be used if haematin/haem arginate is not immediately available



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Next question >

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Links

Royal College of Physicians

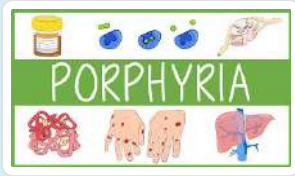
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[2012 The acute porphyrias](#)



[Suggest link](#)

[Report broken link](#)

Media





Porphyria

Townsend Teaching - YouTube  4  0





Acute intermittent porphyria

Osmosis - YouTube  17  3



Acute Intermittent Porphyria

Pixorize - YouTube  2  1

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A 34-year-old woman is rushed to the emergency department by her husband. Her husband says that she has been lethargic for the last 2 days and this morning has become increasingly more confused and behaving differently to normal. She has no past medical history of note. She is 16 weeks pregnant.

On examination, she is febrile with a temperature of 38.5°C. She is tachycardic with a heart rate of 125 bpm and has a blood pressure of 115/95mmHg. On auscultation, her chest is clear with normal heart sounds. Her abdomen is soft and non-tender with a palpable uterus in keeping with 16 weeks gestation.

Investigations:

Hb	92 g/L	Male: (135-180) Female: (115 - 160)
Platelets	43 * 10 ⁹ /L	(150 - 400)
WBC	6.3 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	3.8 mmol/L	(3.5 - 5.0)
Urea	11.2 mmol/L	(2.0 - 7.0)
Creatinine	185 µmol/L	(55 - 120)
Bilirubin	32 µmol/L	(3 - 17)
ALP	35 u/L	(30 - 100)
ALT	85 u/L	(3 - 40)
Albumin	37 g/L	(35 - 50)
CRP	< 1 mg/L	(< 5)

Urinalysis: negative.

Pregnancy test: positive.

What is the next immediate treatment for this patient?

- ☐ Intravenous antibiotics ×
- ☐ Intravenous immunoglobulin ×
- ☐ Magnesium sulphate ×

- ☐ Plasma exchange
- ☐ Platelet transfusion

Submit answer

Reference ranges ▾

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ALP	35 u/L	(30 - 100)
ALT	85 u/L	(3 - 40)
Albumin	37 g/L	(35 - 50)
CRP	< 1 mg/L	(< 5)

Urinalysis: negative.

Pregnancy test: positive.

What is the next immediate treatment for this patient?

Intravenous antibiotics	2%
Intravenous immunoglobulin	16%
Magnesium sulphate	8%

Plasma exchange

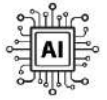
72%

Platelet transfusion

2%

TTP - plasma exchange is first-line

Important for me **Less important**



The pentad of symptoms: AKI, fever, cerebral dysfunction, thrombocytopenia and microangiopathic haemolytic anaemia should point towards a diagnosis of thrombotic thrombocytopenic purpura (TTP). TTP is a serious condition that causes dysregulation of the clotting cascade. The underlying mechanism is not completely understood but a deficiency in the enzyme ADAMTS13 has been identified. If left untreated, TTP has a high mortality. Pregnancy is a known cause of TTP although it does not have to be present to make the diagnosis. If TTP is suspected, the first-line treatment of choice is plasma exchange. Plasma exchange removes any antibodies which inhibit ADAMTS13 whilst also replacing the functioning version of the enzyme. Steroids and rituximab have also been used to suppress the patient's immune system from producing enzymes to ADAMTS13.

Intravenous antibiotics are an appropriate consideration, given that this patient is febrile. In the absence of raised inflammatory markers, it seems more likely that fever is a symptom of TTP rather than an underlying infection. Nevertheless, even if given, antibiotic administration will not treat TTP.

Intravenous immunoglobulin is used in the treatment of refractory TTP. However, it is not the first-line treatment of choice.

Magnesium sulphate is used in the treatment of eclampsia. It is not used in the treatment of TTP.

Platelet transfusion is not recommended in TTP. Transfusion is associated with an increased risk of thrombosis and mortality.



Discuss (6)

Improve

Next question >

Thrombotic thrombocytopenic purpura: management ★

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels

- in TTP there is a deficiency of protease which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management

- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine



123



Next question >

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Textbooks

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Links

British Journal of Haematology

[2012 TTP guidelines](#)



4



4

[Suggest link](#)

[Report broken link](#)

Score: **12%**

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A 28-year-old man is admitted to the Medical Admissions Unit with a 2-day history of itching, right upper quadrant pain, and abdominal distension. The pain started as a dull ache but became constant and severe over the course of several hours.

His past medical history is remarkable only for a left lower limb DVT diagnosed at age 20. He takes no regular medications and he is a non-smoker. He drinks 2-3 units of alcohol per week and denies intravenous drug use.

Examination reveals a jaundiced young man with pale conjunctivae. He appears deeply uncomfortable. His abdomen is moderately distended with marked right upper quadrant tenderness. His liver and spleen are both palpable 2cm below the costal margin. Shifting dullness is demonstrable on percussion of the abdomen.

His blood results are as follows:

Hb	101 g/l	Na ⁺	139 mmol/l	Bilirubin	109 µmol/l
MCV	102.4 fl	K ⁺	4.2 mmol/l	ALP	284 u/l
Platelets	63 * 10 ⁹ /l	Urea	6.7 mmol/l	ALT	684 u/l
WBC	12.9 * 10 ⁹ /l	Creatinine	108 µmol/l	γGT	179 u/l
Neuts	10.8 * 10 ⁹ /l			Albumin	27 g/l
Lymphs	0.9 * 10 ⁹ /l			LDH	759 u/l

His abdominal ultrasound scan is consistent with hepatic vein thrombosis and the patient is started on low molecular weight heparin. Following a review by the Haematologists, a diagnosis of paroxysmal nocturnal haemoglobinuria is made and the patient is advised to start treatment with eculizumab.

Given the proposed treatment strategy, which of the following vaccinations should the patient be offered?

<input type="radio"/> Hepatitis B	×
<input type="radio"/> Neisseria meningitidis	×
<input type="radio"/> Varicella zoster virus	×
<input type="radio"/> Streptococcus pneumoniae	×

☐ Haemophilus influenzae type b



Submit answer

Reference ranges ▾

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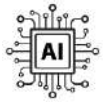
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Given the proposed treatment strategy, which of the following vaccinations should the patient be offered?

Hepatitis B	12%
Neisseria meningitidis	33%
Varicella zoster virus	9%
Streptococcus pneumoniae	23%



Eculizumab is a recombinant humanised monoclonal antibody that specifically binds to terminal complement protein C5. Patients with C5 deficiency are at elevated risk of serious meningococcal infections and all patients being treated with eculizumab should receive a quadrivalent vaccine against the meningococcal strains A, C, W, and Y.

[Discuss \(2\)](#)[Improve](#)[Next question >](#)

Paroxysmal nocturnal haemoglobinuria ★

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

Pathophysiology

- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

Features

- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

Diagnosis

- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

Management

- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation



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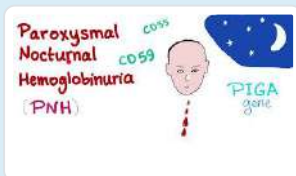


Textbooks

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Media



Paroxysmal Nocturnal Hemoglobinuria

Medicosis Perfectionalis - YouTube



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A 32-year-old male presents with a progressive worsening non-specific lethargy. 9 months ago, he had returned from an active holiday from New Zealand and now feels lethargic to the point that he can no longer work in his job as a computer programmer. In this period, he has been treated for two deep vein thromboses with low molecular heparin, the first initially attributed to his return flight from New Zealand. He reports three episodes of rose coloured urine over the past 4 months and intermittent episodes of abdominal cramps that his GP had diagnosed to be irritable bowel syndrome.

On examination, you note mild conjunctival pallor and jaundiced sclera. Respiratory, cardiovascular and abdominal examinations are unremarkable. His blood results are as follows:

Hb	76 g/l
MCV	92 fl
Platelets	$276 \times 10^9/l$
WBC	$4.1 \times 10^9/l$
Reticulocytes	18%
Haptoglobin	2 (normal range 41-165 mg/dL)
LDH	2128 (normal range 140-280 units/L)
Coombs' test	negative at 4 and 37 degrees

What is the definitive treatment for the underlying condition?

- ☐ Packed red blood cell transfusion ×
- ☐ Anti-retroviral treatment ×
- ☐ Bone marrow transplant ×
- ☐ R-CHOP chemotherapy ×
- ☐ Intravenous iron replacement ×

Submit answer

Reference ranges

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Question 38 of 191



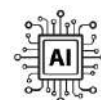
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Haptoglobin	2 (normal range 41-165 mg/dL)
LDH	2128 (normal range 140-280 units/L)
Coombs' test	negative at 4 and 37 degrees

What is the definitive treatment for the underlying condition?




Packed red blood cell transfusion	15%
Anti-retroviral treatment	9%
Bone marrow transplant	49%
R-CHOP chemotherapy	22%
Intravenous iron replacement	4%



This is a tricky clinical scenario with a number of red herrings: a young man in his 30s has presented with recurrent DVTs, episodes of haematuria, abdominal cramps and a blood picture suggestive of intravascular haemolysis (low haptoglobin, raised LDH) not secondary to an

autoimmune cause (Coombs negative): there is thus an underlying red cell fragility predisposing to thrombosis, strongly suggestive of paroxysmal nocturnal haemoglobinuria (PNH). Note that haemoglobinuria is not restricted to night-time alone. The majority of patients present in their 30s with thromboses being the most common cause of death.

PNH is caused by an underlying reduced CD 59 on the red cell surface, leading to increased susceptibility to complement lysis. Complications can present following the release of haemoglobin, such as pulmonary hypertension, dystonia and renal impairment while PNH can overlap with aplastic anaemia and myelodysplasia. PNH patients are managed by blocking complement lysis with eculizumab and red cell transfusions but the only curative solution is allogenic bone marrow transplantation.

		 Discuss (4)	Improve
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Next question >

Paroxysmal nocturnal haemoglobinuria ★

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

Pathophysiology

- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

Features

- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

Diagnosis

- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH

- Ham's test: acid-induced haemolysis (normal red cells would not)

Management

- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation



123



Next question >

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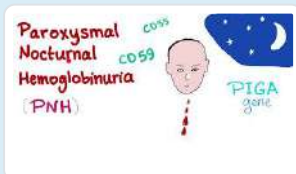


Textbooks

High-yield textbook

Extended textbook

Media



[Paroxysmal Nocturnal Hemoglobinuria](#)

Medicosis Perfectionalis - YouTube



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Question 39 of 191



A 24-year-old female presents with severe abdominal pain. This is her fourth presentation this year. She was previously told that the abdominal pain was medically unexplained. On examination you note peripheral neuropathy of her lower limbs. Her blood pressure is 160/110 mmHg and heart rate 125 beats per minute.

Blood results are as follows:

Hb	115 g/l	Na ⁺	132 mmol/l
Platelets	468 * 10 ⁹ /l	K ⁺	3.8 mmol/l
WBC	14.2 * 10 ⁹ /l	Urea	8.6 mmol/l
Neuts	10.8 * 10 ⁹ /l	Creatinine	72 µmol/l
Lymphs	1.6 * 10 ⁹ /l	CRP	28 mg/l
Eosin	0.2 * 10 ⁹ /l		

Urine	Increased levels of delta aminolevulinic acid and porphobilinogen
-------	---

What treatment is indicated?

- ☐ Dimercaprol ×
- ☐ Penicillamine ×
- ☐ Dimercaptosuccinic acid (DMSA) ×
- ☐ Haem arginate ×
- ☐ Supportive management ×

Submit answer

Reference ranges 

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Lymphs	1.6 * 10 ⁹ /l	CRP	28 mg/l
Eosin	0.2 * 10 ⁹ /l		

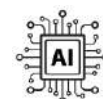
Urine	Increased levels of delta aminolevulinic acid and porphobilinogen
-------	---

What treatment is indicated?

Dimercaprol	4%
Penicillamine	5%
Dimercaptosuccinic acid (DMSA)	16%
Haem arginate	67%
Supportive management	7%

IV haem arginate can be used to treat flares of acute intermittent porphyria

Important for me Less important





The clinical features and laboratory data are suggestive of acute intermittent porphyria (AIP). This is one of the hereditary hepatic porphyrias. Its inheritance is autosomal dominant. The deficient enzyme is porphobilinogen deaminase (PBGD). A deficiency of PBGD is not sufficient by itself to produce AIP, and other activating factors must also be present. These include hormones, drugs

and dietary changes.

Hematin and heme arginate is the treatment of choice during an acute attack of AIP. Heme is not a curative treatment, but can shorten attacks and reduce the intensity of an attack.

Dimercaprol, penicillamine and dimercaptosuccinic acid (DMSA) can be used to treat lead toxicity. Lead toxicity can present similarly to AIP (e.g. abdominal pain and peripheral neuropathy). In lead poisoning we would expect increased urinary coproporphyrin.

		 Discuss (5)	Improve
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Next question >

Acute intermittent porphyria ★

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40-year-olds. AIP is more common in females (5:1)

The classical presentation is a combination of abdominal, neurological and psychiatric symptoms:

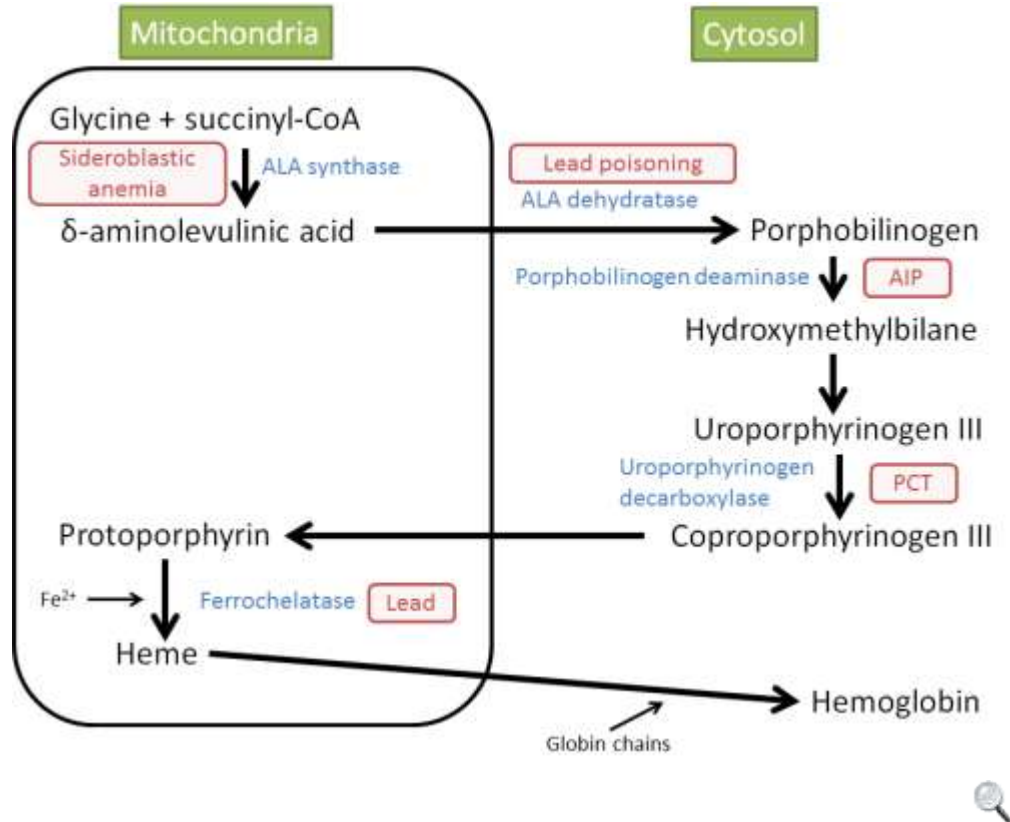
- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

Diagnosis

- classically urine turns deep red on standing
- raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
- assay of red cells for porphobilinogen deaminase
- raised serum levels of delta aminolaevulinic acid and porphobilinogen

Management

- avoiding triggers
- acute attacks
 - IV haematin/haem arginate
 - IV glucose should be used if haematin/haem arginate is not immediately available



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123



Next question >

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Textbooks

High-yield textbook

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Links

Royal College of Physicians

[2012 The acute porphyrias](#)



9



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[Suggest link](#)

[Report broken link](#)

Media





Porphyria

Townsend Teaching - YouTube  4  0





Acute intermittent porphyria

Osmosis - YouTube  17  3



Acute Intermittent Porphyria

Pixorize - YouTube  2  1

[Report broken media](#)

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Question 40 of 191



A 30-year-old woman presents to the emergency department with severe, progressive abdominal pain over the past day. The pain is accompanied by nausea, vomiting and diarrhoea. The patient recalls similar episodes in the past that progressed over a few days and lasted for a week. Temperature is 37°C, blood pressure is 140/100 mmHg, pulse is 120/min and respirations are 16/min.

On examination: minimal abdominal tenderness and rebound tenderness. She has a history of abdominal surgery for suspected appendicitis and biliary disease, neither of which was confirmed once inside the abdomen.

Which of the following will help to confirm the diagnosis?

- | | |
|--|---|
| <input type="radio"/> Erythrocyte porphyrins | × |
| <input type="radio"/> Faecal porphyrins | × |
| <input type="radio"/> Plasma porphyrins | × |
| <input type="radio"/> Urine porphobilinogen | × |
| <input type="radio"/> Urine porphyrins | × |

Submit answer

Reference ranges ▾

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On examination: minimal abdominal tenderness and rebound tenderness. She has a history of abdominal surgery for suspected appendicitis and biliary disease, neither of which was confirmed once inside the abdomen.

Which of the following will help to confirm the diagnosis?

Erythrocyte porphyrins	1%
Faecal porphyrins	1%
Plasma porphyrins	3%
Urine porphobilinogen	85%
Urine porphyrins	10%

In acute intermittent porphyria, urinary porphobilinogen is typically raised

Important for me Less important



This patient has acute intermittent porphyria, which classically presents with neurovisceral symptoms which can mimic an acute abdomen. This mimicry occurs because the abdominal pain is produced by a nerve problem rather than inflammation, hence why exploratory surgery is uneventful. In long-standing cases, patients may have damage to their motor nerves resulting in upper limb weakness.

Acute intermittent porphyria ★

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40-year-olds. AIP is more common in females (5:1)

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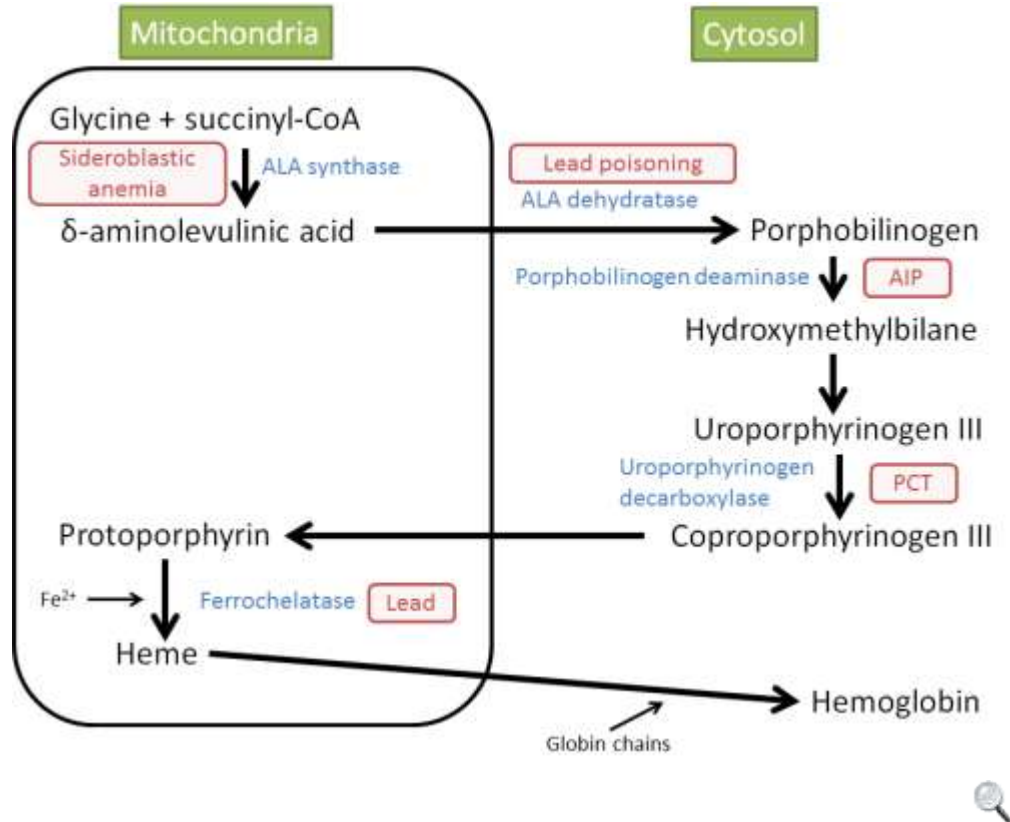
- abdominal: abdominal pain, vomiting
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- psychiatric: e.g. depression
- hypertension and tachycardia common

Diagnosis

- classically urine turns deep red on standing
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Management

- avoiding triggers
- acute attacks
 - IV haematin/haem arginate
 - IV glucose should be used if haematin/haem arginate is not immediately available



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Next question >

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Links

Royal College of Physicians

[2012 The acute porphyrias](#)



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Media



Porphyria

Townsend Teaching - YouTube 4 0



Acute intermittent porphyria

Osmosis - YouTube 17 3



Acute Intermittent Porphyria

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Question 41 of 191



A 40-year-old woman of Mediterranean descent was found to be anaemic during a workup for fatigue. Past medical history includes hypothyroidism, which is currently well controlled on 125mcg levothyroxine, and hypertension for which she takes amlodipine 5mg.

She denies any recent weight loss or change in bowel habits and her periods remain regular and are no heavier than normal. Blood tests results showed:

Hb	85g/l	115-165g/l
MCV	60fL	79-95fL
Iron	32nmol/L	13-32nmol/l
Ferritin	250µg/l	11-307µg/l
TIBC	50µmol/l	45-70µmol/l
Folate	2.5µg/l	3.1-19.9µg/l
B12	253ng/l	145-910ng/l

Which test is most likely to identify the underlying cause of her anaemia?

- ☐ Anti-tissue transglutaminase (anti-tTG) antibodies ×
- ☐ Colonoscopy ×
- ☐ Prussian blue stain ×
- ☐ Haemoglobin electrophoresis ×
- ☐ Blood film ×

Submit answer

Reference ranges 

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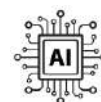
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TIBC	50µmol/l	45-70µmol/l
Folate	2.5µg/l	3.1-19.9µg/l
B12	253ng/l	145-910ng/l

Which test is most likely to identify the underlying cause of her anaemia?

Anti-tissue transglutaminase (anti-tTG) antibodies	14%
Colonoscopy	1%
Prussian blue stain	6%
Haemoglobin electrophoresis	68%
Blood film	11%

Disproportionately low MCV think thalassaemia

Important for me Less important







The differential diagnosis for microcytic anaemias includes iron deficiency anaemia (IDA), thalassaemia, and sideroblastic anaemia. Colonoscopy is used to investigate unexplained IDA but serum iron and ferritin levels were raised in this patient, thus excluding IDA.

The disproportionately low MCV compared with haemoglobin levels points towards thalassaemia

where iron and ferritin levels can often be normal or high. Whilst a blood film would aid the diagnosis, HbA2 >3.5% on haemoglobin electrophoresis is diagnostic.

Prussian blue stains are used in the diagnosis of sideroblastic anaemia but one would expect significantly raised iron levels and reduced TIBC.

Anti-tTGs are used in the diagnosis of coeliac disease which often causes a mixed iron and folate deficiency. Whilst folate levels are low in this patient, this can also be explained by a chronic background level of haemolysis in thalassaemia and the other results are not in keeping with a coeliac picture.

   Discuss (5)  Improve

Next question >

Microcytic anaemia ★

Causes

- iron-deficiency anaemia
- thalassaemia*
- congenital sideroblastic anaemia
- anaemia of chronic disease (more commonly a normocytic, normochromic picture)
- lead poisoning






A question sometimes seen in exams gives a history of a normal haemoglobin level associated with a microcytosis. In patients not at risk of thalassaemia, this should raise the possibility of polycythaemia rubra vera which may cause an iron-deficiency secondary to bleeding.

New onset microcytic anaemia in elderly patients should be urgently investigated to exclude underlying malignancy.

*in beta-thalassaemia minor the microcytosis is often disproportionate to the anaemia



Next question >

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Textbooks

High-yield textbook

Extended textbook

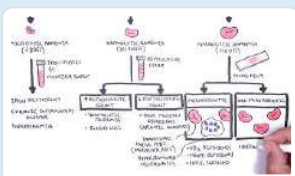
Media



Anemia (Types, Lab Findings, High Yield Images)

DirtyUSMLE - YouTube

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Anaemia (anemia) - classification (microcytic, normocytic and macrocytic) and pathophysiology

Armando Hasudungan - YouTube

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Question 42 of 191



A 46-year-old man with a diagnosis of chronic hepatitis C is reviewed in hepatology clinic. He complains of 3 weeks of lethargy and generalised muscle pain.

On examination there are erythematous macules and purpuric papules on both lower limbs with some small areas of ulceration. Light touch and pain sensation is reduced in the toes bilaterally.

What is the most likely cause of these symptoms?

- ☐ Eosinophilic granulomatosis with polyangiitis ×
- ☐ Leukocytoclastic vasculitis ×
- ☐ Granulomatosis with polyangiitis ×
- ☐ Cryoglobulinaemia ×
- ☐ Microscopic polyangiitis ×

Submit answer

Reference ranges 

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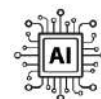
On examination there are erythematous macules and purpuric papules on both lower limbs with some small areas of ulceration. Light touch and pain sensation is reduced in the toes bilaterally.

What is the most likely cause of these symptoms?

Eosinophilic granulomatosis with polyangiitis	1%
Leukocytoclastic vasculitis	4%
Granulomatosis with polyangiitis	2%
Cryoglobulinaemia	90%
Microscopic polyangiitis	4%

Hepatitis C is associated with mixed (type II) cryoglobulinaemia

Important for me Less important



A vasculitic rash and neuropathy in a patient with hepatitis C is suggestive of cryoglobulinaemia.

Small-vessel vasculitides can all cause neuropathy, however the association with hepatitis C makes cryoglobulinaemia most likely.

Patients with eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome) typically present with a history of allergic rhinitis and asthma. The disease progresses to eosinophilic infiltrative disease (eg, eosinophilic pneumonia or gastroenteritis) and systemic medium- and small-vessel vasculitis with granulomatous inflammation.

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis has a spectrum of presentations but often includes chronic sinusitis (failure to respond to conventional treatment is suggestive). Rhinitis and epistaxis occur in 22% and 11% of patients with GPA, respectively.

Fauci AS, Haynes BS, Katz P, Wolff SM. Wegener's granulomatosis: prospective clinical and therapeutic experience with 85 patients for 21 years. Ann Intern Med. January 1983. 98(1):76-85



Discuss (5)

Improve

Next question >

Cryoglobulinaemia ★

Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C. One-third of cases are idiopathic

Three types

- type I (25%):
 - monoclonal - IgG or IgM
 - associations: multiple myeloma, Waldenstrom macroglobulinaemia
- type II (25%)
 - mixed monoclonal and polyclonal: usually with rheumatoid factor
 - associations: hepatitis C, rheumatoid arthritis, Sjogren's, lymphoma
- type III (50%)
 - polyclonal: usually with rheumatoid factor
 - associations: rheumatoid arthritis, Sjogren's

Possible features

- Raynaud's only seen in type I
- cutaneous
 - vascular purpura
 - distal ulceration
 - ulceration
- arthralgia
- renal involvement
 - diffuse glomerulonephritis

Investigations

- low complement (esp. C4)
- high ESR

Management

- treatment of underlying condition e.g. hepatitis C
- immunosuppression

- plasmapheresis



123



Next question >

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Textbooks

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A 65-year-old man attends the Emergency Department with a one-month history of persistent left-sided chest pain that is unresponsive to analgesia. He describes the pain as a constant ache, which does not worsen with exertion or radiate elsewhere. His medical background includes hypertension and diabetes, and he has a significant smoking history. His current medication regimen comprises enalapril, metformin, vildagliptin, and glimepiride.

Hb	110 g/L	Male: (135-180)
Platelets	$210 \times 10^9/L$	(150 - 400)
WBC	$6.4 \times 10^9/L$	(4.0 - 11.0)
Calcium	2.8 mmol/L	(2.1-2.6)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.4 mmol/L	(3.5 - 5.0)
Urea	7.2 mmol/L	(2.0 - 7.0)
Creatinine	235 $\mu\text{mol/L}$	(55 - 120)

No cardiac abnormalities were detected on ECG or echocardiography.

What is the most appropriate imaging modality for this patient?

☐ Bone scan
 ×

☐ Chest x-ray
 ×

☐ PET-CT
 ×

☐ Skeletal survey
 ×

☐ Whole body MRI
 ×

Submit answer

Reference ranges 

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Urea	7.2 mmol/L	(2.0 - 7.0)
Creatinine	235 µmol/L	(55 - 120)

No cardiac abnormalities were detected on ECG or echocardiography.

What is the most appropriate imaging modality for this patient?

Bone scan	11%
Chest x-ray	23%
PET-CT	14%
Skeletal survey	15%
Whole body MRI	36%

Whole body MRI 1st line imaging in suspected multiple myeloma

Important for me Less important

Whole body MRI is the correct answer. The constellation of symptoms, including left-sided chest pain (bony aches), anaemia, hypercalcaemia, and renal impairment, should prompt consideration of multiple myeloma. Whole-body MRI is the recommended modality for diagnosis when multiple myeloma is suspected, as per NICE and BSH guidelines. Diagnostic features of myeloma on MRI include a diffuse pattern of bone marrow involvement and numerous focal lesions throughout the

skeleton. These lesions typically present with a 'salt-and-pepper' appearance due to varying signal intensities caused by active myeloma cells and fatty marrow replacement.

Bone scan is not the appropriate choice. Although bone scans use a radioactive tracer to evaluate bone metabolism, they are limited in detecting small focal lesions and do not adequately assess bone marrow involvement in multiple myeloma. Furthermore, they may demonstrate nonspecific uptake in other conditions affecting bone remodelling and repair.

Chest x-ray, while capable of revealing osteolytic lesions, does not provide sufficient information to differentiate between multiple myeloma and metastatic disease; thus, it is not advocated for definitive diagnosis.

PET-CT, although an alternative diagnostic tool for patients with newly diagnosed nonsecretory or oligo secretory multiple myeloma or those presenting with the extramedullary disease, lacks sufficient evidence to support its routine use in all cases of newly diagnosed multiple myeloma. One limitation is the potential for high false positive and false negative findings rates.

Skeletal survey is less sensitive than CT, MRI, and PET/CT; therefore, it is considered suboptimal and is not advisable in this clinical scenario.



Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
 - much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
 - this leads to constipation, nausea, anorexia and confusion
- Renal

- monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
- this causes renal damage which presents as dehydration and increasing thirst
- other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- ## Diagnostic criteria

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

Next question >

Textbooks

High-yield textbook

Extended textbook

Links

Haematological cancers - recognition and referral

NICE

👍 12 🗑️ 6

2016 myeloma guidelines

[Suggest link](#)

[Report broken link](#)

Media



Multiple Myeloma - Diagnosis and Treatment

Medicosis Perfectionalis - YouTube

👍 6 🗑️ 0



Multiple Myeloma

Medicosis Perfectionalis - YouTube

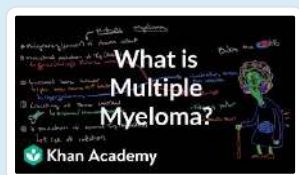
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Multiple Myeloma Mnemonic...the story of the plasma cell

Medicosis Perfectionalis - YouTube

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What is multiple myeloma?

Khan Academy - YouTube

👍 4 🗑️ 1



Multiple Myeloma

Townsend Teaching - YouTube

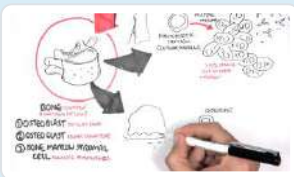
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Multiple Myeloma

CRASH! Medical Review - YouTube

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Multiple Myeloma

Armando Hasudungan - YouTube

👍 1 🗨️ 3

[Report broken media](#)

Score: **12%**

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An 18-year-old woman presents to the emergency department with dark urine. She had recently been diagnosed with 'mono' following a sore throat confirmed by swab testing, originally becoming unwell nine days ago. She had been recovering and was starting to feel well but then noticed passing dark urine after having a walk outside in the park but she started to return after it started to rain heavily and she became very cold. She also had abdominal cramping sensation. She has no other past medical history, takes no medication apart from the oral contraceptive pill, and has no allergies.

Blood tests:

Hb	101 g/l
Platelets	$379 \times 10^9/l$
WBC	$5.1 \times 10^9/l$
Bilirubin	43 $\mu\text{mol/l}$
ALP	161 u/l
ALT	15 u/l
Blood film	spherocytes

What is the most appropriate investigation to establish a diagnosis?

- ☐ Hepatitis C serology ×
- ☐ Syphilis serology ×
- ☐ Anti-nuclear antibody ×
- ☐ Direct Coombs test ×
- ☐ ESO titre ×

Submit answer

Reference ranges 

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Blood tests:

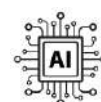
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WBC	$5.1 \times 10^9/l$
Bilirubin	43 $\mu\text{mol/l}$
ALP	161 u/l
ALT	15 u/l
Blood film	spherocytes

What is the most appropriate investigation to establish a diagnosis?

Hepatitis C serology	7%
Syphilis serology	1%
Anti-nuclear antibody	1%
Direct Coombs test	78%
ESO titre	14%

Paroxysmal cold haemoglobinuria should be confirmed with urinary heamosiderin

Important for me Less important



This is a young patient who has developed dark urine associated with exposure to going outside, implying exposure to cold. This has been associated with abdominal cramps and following a recent viral infection, most likely with Epstein-Barr virus. In addition, blood tests show anaemia,

elevated bilirubin and spherocytes. This implies haemolysis, and the history suggests that the haemolysis is associated after cold exposure. This history suggests is typical for paroxysmal cold haemoglobinuria. Paroxysmal cold haemoglobinuria is due to cold-reacting IgG causing complement fixation leading to haemolysis.

Diagnosis is best established with direct Coombs test to demonstrate the intravascular nature of haemolysis. Further testing can demonstrate the presence of temperature specific IgG antibodies which react to red blood cells below 37 degrees C and cause hemolysis on re-warming. Syphilis was historically associated with this condition, but only in tertiary syphilis which such a young patient is unlikely to have. Determining ESO titre to establish the viral infection is unlikely to be helpful in the current situation, and whilst hepatitis C is associated with cryoglobulinaemia it is not associated with paroxysmal cold haemoglobinuria. In older patients, paroxysmal cold haemoglobinuria can be associated with auto-immune conditions, making ANA a useful screening test, but there is no chronic history suggesting a prolonged autoimmune condition.



Discuss (15)

Improve

Next question >

Paroxysmal nocturnal haemoglobinuria ★

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

Pathophysiology

- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

Features

- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

Diagnosis

- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

Management

- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation



123



Next question >

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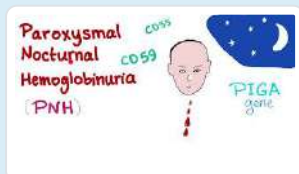


Textbooks

High-yield textbook

Extended textbook

Media



[Paroxysmal Nocturnal Hemoglobinuria](#)

Medicosis Perfectionalis - YouTube



9



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[Report broken media](#)

Score: **12%**

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A 74-year-old man attends with worsening fatigue and shortness of breath. A systematic enquiry was otherwise unremarkable. He was treated with radical chemo-radiotherapy for metastatic squamous cell carcinoma 5 years ago.

Blood results are as follows:

Hb	72 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$42 \times 10^9/L$	(150 - 400)
WBC	$2.1 \times 10^9/L$	(4.0 - 11.0)
Neuts	$0.4 \times 10^9/L$	(2.0 - 7.0)
Lymphs	$0.6 \times 10^9/L$	(1.0 - 3.5)
Mono	$1.0 \times 10^9/L$	(0.2 - 0.8)
Eosin	$0.1 \times 10^9/L$	(0.0 - 0.4)

Blood film	Occasional hypogranular and hypolobulated neutrophil; Blasts 8% of all nucleated cells
------------	--

What is the most likely diagnosis?

- ☐ Acute lymphoblastic leukaemia ×
- ☐ Acute myeloid leukaemia ×
- ☐ Metastatic infiltration ×
- ☐ Myelodysplastic syndrome ×
- ☐ Myelofibrosis ×

Submit answer

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Question 45 of 191



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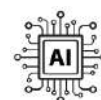
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What is the most likely diagnosis?

Acute lymphoblastic leukaemia	5%
Acute myeloid leukaemia	19%
Metastatic infiltration	15%
Myelodysplastic syndrome	44%
Myelofibrosis	16%

Pancytopenia 5 years post-chemotherapy/radiotherapy → ?myelodysplastic syndrome

Important for me Less important



Myelodysplastic syndrome is correct. The patient most likely has therapy-related myelodysplastic syndromes (t-MDS) which is defined as MDS occurring as a complication of cytotoxic chemotherapy and/or radiation. The median onset of occurrence is 5 years post-chemotherapy




(however this can vary widely with the type of chemotherapy given). The blood film appearances of hypogranular and hypolobulated neutrophils are classic of MDS. The presence of myeloblasts is also in keeping with this condition, and since the blast count is $< 20\%$ on peripheral blood the diagnosis is MDS rather than acute myeloid leukaemia. The patient requires an urgent bone marrow aspirate and trephine for morphology, cell markers, and cytogenetics.

Acute lymphoblastic leukaemia is incorrect. Acute lymphoblastic leukaemia (ALL) is rare in adults. It is predominantly a disease of children. The blood film appearances are not in keeping with ALL which would present with lymphoblasts and the absence of dysplasia in the myeloid lineage.

Acute myeloid leukaemia is incorrect. The peripheral blast count is $< 20\%$ confirming a diagnosis of MDS. Acute myeloid leukaemia (AML) is characterised by a peripheral blast count $> 20\%$. It is important to note that the main risk of MDS is transformation to AML.

Metastatic infiltration is incorrect. Metastatic infiltration would be characterised by leukoerythoblastosis and teardrop poikilocytes on the blood film.

Myelofibrosis is incorrect. Myelofibrosis would also be characterised by leukoerythoblastosis and teardrop poikilocytes on the blood film.

		 Discuss (2)	Improve
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Next question >

Myelodysplastic syndrome ★

Myelodysplastic syndromes (MDS) encompass a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, peripheral blood cytopenias, and a risk of progression to acute myeloid leukaemia (AML). These disorders predominantly affect older adults, with a median age at diagnosis of 70-75 years.

Aetiology and Pathophysiology

MDS arises from genetic mutations in hematopoietic stem cells.

Around 90% of cases are primary with the remaining 10% secondary to causes such as chemotherapy and radiotherapy. Secondary MDS typically develops around 5 years post-treatment.

The key pathophysiological feature of MDS is ineffective hematopoiesis leading to peripheral cytopenias despite a typically hypercellular bone marrow. The exact mechanisms are still not entirely understood, but they likely involve a combination of increased apoptosis, abnormal differentiation, and immune dysregulation.

Clinical Features

MDS can present with various symptoms related to the underlying cytopenias. Common presentations include fatigue, weakness, and pallor due to anaemia; recurrent infections due to neutropenia; and easy bruising or bleeding due to thrombocytopenia. Some patients may be asymptomatic and are diagnosed incidentally on routine blood counts.

Diagnosis

The diagnosis of MDS is based on peripheral blood counts, bone marrow examination, and cytogenetic analysis. Bone marrow biopsy typically shows dysplastic changes in hematopoietic cells and a varying degree of blasts. Cytogenetic analysis can identify specific chromosomal abnormalities that may have prognostic implications.

Treatment


Treatment of MDS depends on the subtype of MDS, the patient's age and overall health, and the severity of symptoms. Options include supportive care (e.g., blood transfusions, growth factors), disease-modifying therapy (e.g., hypomethylating agents, lenalidomide), immunosuppressive therapy, and hematopoietic stem cell transplantation. The latter is the only potentially curative option but is limited by the patient's age and comorbidities.

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Next question >

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Textbooks



High-yield textbook

Extended textbook

Media



Myelodysplastic syndromes

Osmosis - YouTube  9  0

[Report broken media](#)

Score: **12%**

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Question 46 of 191



A 45-year-old gentleman has a diagnosis of renal cell carcinoma and is booked for a nephrectomy in four days time. He presents with an acutely swollen, tender left calf and a diagnosis of deep vein thrombosis is made, with the ultrasound report describing a clot extending to the femoral vein. Which management is most appropriate?

- ☐ Low molecular weight heparin and IVC filter insertion ×
- ☐ Low molecular weight heparin ×
- ☐ Warfarin ×
- ☐ Apixiban ×
- ☐ None ×

Submit answer

Reference ranges 

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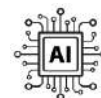
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A 45-year-old gentleman has a diagnosis of renal cell carcinoma and is booked for a nephrectomy in four days time. He presents with an acutely swollen, tender left calf and a diagnosis of deep vein thrombosis is made, with the ultrasound report describing a clot extending to the femoral vein. Which management is most appropriate?

Low molecular weight heparin and IVC filter insertion	41%
Low molecular weight heparin	27%
Warfarin	2%
Apixiban	29%
None	1%

If a diagnosis of DVT is made less than 7 days before surgery, an IVC filter must be inserted pre-op

Important for me Less important



This gentleman has a malignancy that needs urgent operative management. An IVC filter should be inserted pre-operatively to bridge the operative period when low molecular weight heparin will be held.

The British Society of Haematology recommends that 'IVC filters should be considered in any pre-operative patient with recent VTE (within 1 month) in whom anticoagulation must be interrupted'.

Whilst DOACs such as apixaban are now recommended first-line for venous thromboembolism they would be less suitable as surgery is planned in 4 days time.





 Discuss (4)

 Improve

Next question >

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered

- If a DVT is 'unlikely' (1 point or less)

- ## D-dimer tests

- [illegible]

The cornerstone of VTE management is anticoagulant therapy. This was historically done with warfarin, often preceded by heparin until the INR was stable. However, the development of DOACs, and an evidence base supporting their efficacy, has changed modern management.

- the big change in the 2020 guidelines was the increased use of DOACs
- apixaban or rivaroxaban (both DOACs) should be offered first-line following the diagnosis of a DVT

- instead of using low-molecular weight heparin (LMWH) until the diagnosis is confirmed, NICE now advocate using a DOAC once a diagnosis is suspected, with this continued if the diagnosis is confirmed
- if neither apixaban or rivaroxaban are suitable then either LMWH followed by dabigatran or edoxaban OR LMWH followed by a vitamin K antagonist (VKA, i.e. warfarin)
- if the patient has active cancer
 - previously LMWH was recommended
 - the new guidelines now recommend using a DOAC, unless this is contraindicated
- if renal impairment is severe (e.g. $< 15/\text{min}$) then LMWH, unfractionated heparin or LMWH followed by a VKA
- if the patient has antiphospholipid syndrome (specifically 'triple positive' in the guidance) then LMWH followed by a VKA should be used

Length of anticoagulation

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer at increased risk
 - an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Links

NICE

👍 25 👎 9

2020 Venous thromboembolism guidelines

Suggest link

[Report broken link](#)

Media



Deep vein thrombosis

Osmosis - YouTube

3 0



Understanding Deep Vein Thrombosis (DVT)

Zero To Finals - YouTube

👍 2 👎 1



Deep Vein Thrombosis - Overview (pathophysiology, treatment, complications)

Armando Hasudungan - YouTube

👍 3 👎 2

[Report broken media](#)

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A 34-year-old woman presents to the emergency department with fever and bruising. She has no past medical history and does not take any regular medications. She does not smoke or drink alcohol and works as an accountant.

Observations:

- Heart rate 94 beats per minute
- Temperature 38.1°C
- Blood pressure 170/101 mmHg
- Respiratory rate 18/minute
- Oxygen saturations 96% on room air

On examination, there is no meningism. You note that she is jaundiced but there are no signs of chronic liver disease. There are scattered petechiae on her arms, legs and abdomen.

Bloods tests:

Hb	72 g/L	Male: (135-180) Female: (115 - 160)
MCV	104fL	(80-96)
Platelets	33 * 10 ⁹ /L	(150 - 400)
WBC	4.6 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	136 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	9.2 mmol/L	(2.0 - 7.0)
Creatinine	155 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	53 µmol/L	(3 - 17)
ALP	88 u/L	(30 - 100)
ALT	24 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	36 g/L	(35 - 50)
Prothrombin time	11 seconds	(10-14)

Blood film	schistocytes
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ADAMTS13 enzyme	absent
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Urinalysis:

Protein	++
Blood	++
Leucocytes	+
Nitrites	-ve
Glucose	-ve

Based on the likely diagnosis, what treatment is most likely to be effective?

- ☐ Antibiotics ×
- ☐ Antiplatelet therapy ×
- ☐ High dose intravenous steroids ×
- ☐ Intravenous labetalol ×
- ☐ Plasma exchange ×

Submit answer

Reference ranges ∨

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Prothrombin time	11 seconds	(10-14)

Blood film	schistocytes
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ADAMTS13 enzyme	absent
-----------------	--------

Urinalysis:

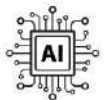
Protein	++
Blood	++
Leucocytes	+
Nitrites	-ve
Glucose	-ve

Based on the likely diagnosis, what treatment is most likely to be effective?

Antibiotics	2%
Antiplatelet therapy	0%
High dose intravenous steroids	18%
Intravenous labetalol	0%
Plasma exchange	80%

TTP - plasma exchange is first-line

Important for me Less important



Plasma exchange is correct. The patient has thrombotic thrombocytopenic purpura as evidenced by fever, thrombocytopenia, renal failure, microangiopathic haemolytic anaemia (jaundice, schistocytes) and absent ADAMTS13 enzyme activity. Haematoproteinuria is also common in this condition. The first-line treatment for this condition is plasma exchange (PEX), which removes inhibitory antibodies and replenishes the deficient protease.





Antiplatelet therapy is incorrect. While this is a thrombotic condition, there is a risk of haemorrhage with antiplatelet treatment.

High dose intravenous steroids is incorrect. Steroids are sometimes administered in this condition but have no proven benefit over PEX alone.

Intravenous labetalol is incorrect. While the patient is hypertensive, the blood pressure is not so high that we would label this as malignant hypertension, which is a differential for a cause of

microangiopathic haemolytic anaemia.

Antibiotics are not the right answer. While no one would criticise someone for administering antibiotics to someone with a petechial rash and fever, on the basis that it could be meningococcal septicaemia, antibiotics have no role in the management of TTP and may even worsen the condition.

   Discuss (5)  Improve

Next question >

Thrombotic thrombocytopenic purpura: management ★

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of protease which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management

- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine



Next question >



B *I*  **A** ▼    ▼ **T** ▼  ▼  

Textbooks

High-yield textbook

Links

British Journal of Haematology

 4  4

[2012 TTP guidelines](#)

[Suggest link](#)

[Report broken link](#)

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Question 48 of 191



A 24-year-old female presents to the emergency department with severe abdominal pain which had developed over for the last few hours. The pain was central, severe and stabbing in nature associated with vomiting. She was in hysterics and was extremely agitated and confused. Past medical history included asthma and depression. Two days earlier she had seen her GP for dysuria and been prescribed trimethoprim.

She was a student studying chemistry at university and had recently been out late several nights drinking excess alcohol to celebrate passing her exams. On examination, she was unwell, extremely clammy, distressed with generalised abdominal tenderness and weakness in both legs with areflexia. Heart sounds and chest were clear. Observations showed a blood pressure 190/100 mmHg, heart rate 126/min, regular and temperature 37.9°C.

Which investigation is most likely to be diagnostic?

- | | |
|---|---|
| <input type="radio"/> Urinary catecholamines | × |
| <input type="radio"/> Abdominal ultrasound | × |
| <input type="radio"/> Urinary porphobilinogen | × |
| <input type="radio"/> Lumbar puncture | × |
| <input type="radio"/> Blood cultures | × |

Submit answer

Reference ranges 

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Which investigation is most likely to be diagnostic?

Urinary catecholamines	4%
Abdominal ultrasound	2%
Urinary porphobilinogen	93%
Lumbar puncture	1%
Blood cultures	0%

In acute intermittent porphyria, urinary porphobilinogen is typically raised

Important for me Less important






This patient has acute intermittent porphyria (AIP). AIP is the most common type of porphyria. AIP is an autosomal dominant condition caused by a genetic mutation in the gene encoding the enzyme porphobilinogen (PBG) deaminase on chromosome 11. The condition is more common in females than males and usually occurs between the ages 14-30 years. Porphyrias occur due to a problem within the haem biosynthesis. Defective PBG deaminase causes PBG to accumulate and this can be found in the urine. Attacks are usually precipitated by drugs, alcohol, fasting and sepsis. This patient's attack has been caused by a combination of antibiotic use and alcohol intake.

Patients most commonly present with gastrointestinal symptoms (most commonly severe

abdominal pain) neurological symptoms (autonomic dysfunction, peripheral motor neuropathies, areflexia, delirium, seizures, coma) and psychiatric symptoms such as common. Observations commonly show tachycardia and hypertension. Fever can be present. Most patients are completely free of symptoms between attacks.

The treatment for acute attacks of porphyria is to decrease haem synthesis and reduce the production of porphyrin precursors. Withdrawal of culprit medication is essential. A high-calorie intake and high doses of glucose can help inhibit haem synthesis and are useful for the treatment of mild attacks. In severe attacks, intravenous haematin is used. Pain is treated with narcotics. Beta blockers can be used to treat tachycardia and hypertension.

Advice can be obtained from National Acute Porphyria Centres: Cardiff, Kings College Hospital, London and Cambridge.

		 Discuss (3)	Improve
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Next question >

Acute intermittent porphyria ★

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40-year-olds. AIP is more common in females (5:1)

The classical presentation is a combination of abdominal, neurological and psychiatric symptoms:

- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

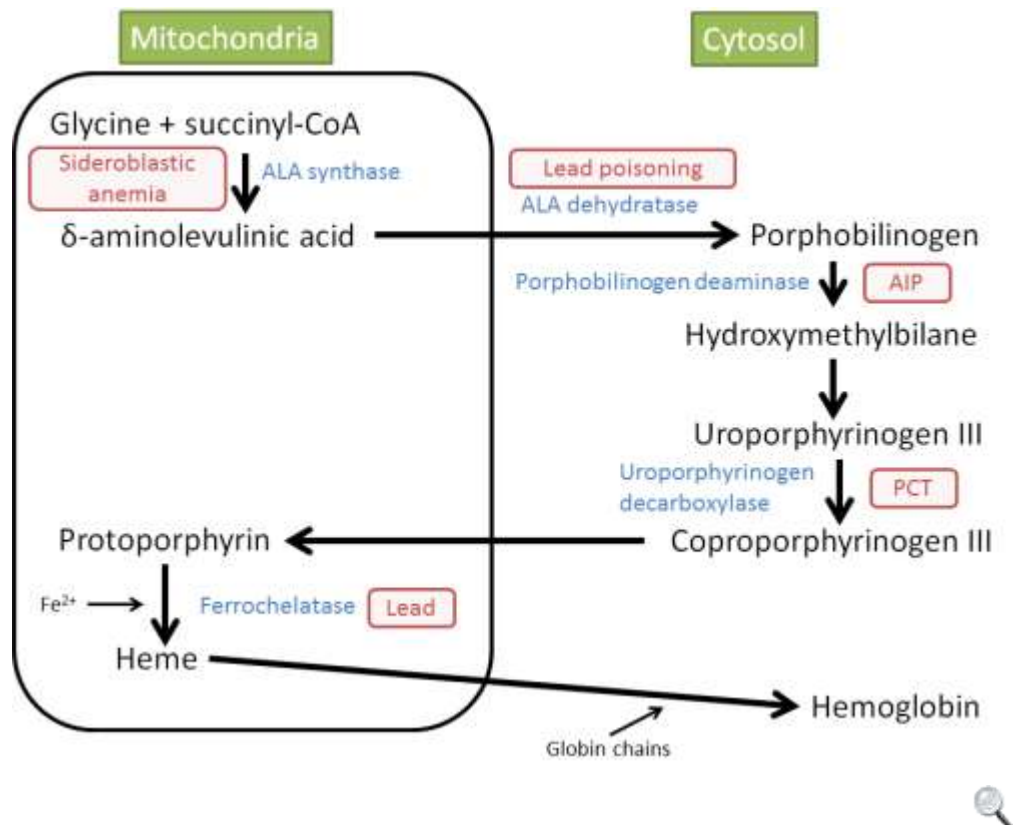
Diagnosis

- classically urine turns deep red on standing
- raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
- assay of red cells for porphobilinogen deaminase
- raised serum levels of delta aminolaevulinic acid and porphobilinogen

Management

- avoiding triggers

- acute attacks
 - IV haematin/haem arginate
 - IV glucose should be used if haematin/haem arginate is not immediately available



AI + Q 123

Next question >

Rich text editor toolbar with icons for Bold (B), Italic (I), Underline (U), Text Color (A), Background Color (■), Bulleted List (≡), Numbered List (1.≡), Indent (≡), Text Color (T), Table (■), Image (🖼️), and Link (🔗).

Textbooks

High-yield textbook

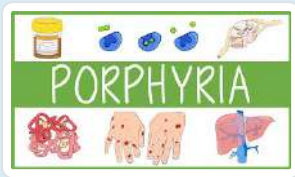
Extended textbook

Links



Royal College of Physicians

👍 9 🗑️ 3

Media





[Porphyria](#)

Townsend Teaching - YouTube  4  0





[Acute intermittent porphyria](#)

Osmosis - YouTube  17  3











[Acute Intermittent Porphyria](#)

Pixorize - YouTube  2  1

[Report broken media](#)

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A 22-year-old man attends with progressive tiredness over the past week. A systematic enquiry was otherwise unremarkable. He has a past medical history of hereditary spherocytosis. His regular medications include folic acid however he states that he often forgets to take this. On examination, you note 5cm splenomegaly.

Blood results are as follows:

Hb	55 g/L	Male: (135-180) Female: (115 - 160)
Platelets	142 * 10 ⁹ /L	(150 - 400)
WBC	14.2 * 10 ⁹ /L	(4.0 - 11.0)
Reticulocytes	0.2 %	(0.5 - 1.5)
Direct antiglobulin test (DAT)	Negative	

Bone marrow examination	Marked erythroid hypoplasia and occasional giant erythroblasts
-------------------------	--

Blood results from the clinic 3 months ago are as follows:

Hb	105 g/L	Male: (135-180) Female: (115 - 160)
Reticulocytes	5.8 %	(0.5 - 1.5)

What is the most likely explanation?

- ☐ Acute erythroblastic leukaemia ×
- ☐ Folic acid deficiency ×
- ☐ Haemolytic crisis ×
- ☐ Parvovirus infection ×
- ☐ Splenic sequestration crisis ×

Submit answer

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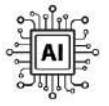
Hb	105 g/L	Male: (135-180) Female: (115 - 160)
Reticulocytes	5.8 %	(0.5 - 1.5)

What is the most likely explanation?

Acute erythroblastic leukaemia	13%
Folic acid deficiency	9%
Haemolytic crisis	7%
Parvovirus infection	51%
Splenic sequestration crisis	20%

Parvovirus infection may trigger an aplastic crisis in patients with hereditary spherocytosis

Important for me Less important



Parvovirus infection is correct. Of note, the patient has significant reticulocytopenia suggestive of bone marrow failure. Two of the commonest causes of this would include infection (e.g. Parvovirus) and megaloblastic anaemia (e.g. B12 and folate deficiency). In health, the usual life span of a red cell is approximately 120 days. However in conditions such as hereditary spherocytosis (HS), due to premature destruction by the spleen, the lifespan could be as low as 10-30 days. Thus acute insults to the bone marrow can manifest much more rapidly in the peripheral blood. Acute parvovirus B19 infection can cause a transient erythroid hypoplasia as demonstrated on the bone marrow results in this case. In healthy populations this would unlikely cause more than mild anaemia, however, in patients with chronic haemolytic states (e.g. red cell membrane disorders and haemoglobinopathies), the effects can be much more rapid and profound as demonstrated in this case.

Acute erythroblastic leukaemia is incorrect. The giant erythroblasts within the bone marrow are indicative of acute parvovirus infection, not leukaemia.

Folic acid deficiency is incorrect. Patients with HS have chronic low-grade haemolysis and therefore an increased red cell turnover. Since folic acid is essential for haematopoiesis, all patients with HS should continue on lifelong folic acid replacement. This is even more essential in a haemolytic crisis. Importantly this remains the case even when folic acid levels are normal. Although the patient, in this case, has poor compliance with folic acid, the bone marrow examination is more suggestive of acute parvovirus infection rather than megaloblastic anaemia.

Haemolytic crisis is incorrect. The presence of a marked reticulocytosis would be suggestive of a haemolytic crisis. However, it would be important to compare this to the patient's baseline reticulocyte count since patients with hereditary spherocytosis will often have chronic reticulocytosis due to low-grade haemolysis of spherocytes. In this case, the patient's reticulocyte count is low, making a haemolytic crisis less likely.

Splenic sequestration crisis is incorrect. Although the patient has mild splenomegaly, this would be expected due to the chronic haemolytic state associated with hereditary spherocytosis. A splenic sequestration crisis would present with a marked and painful enlargement of the spleen.

		Discuss (3)	Improve
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Next question >

Hereditary spherocytosis ★

Basics

- most common hereditary haemolytic anaemia in people of northern European descent
- autosomal dominant defect of red blood cell cytoskeleton
- the normal biconcave disc shape is replaced by a sphere-shaped red blood cell

- red blood cell survival reduced as destroyed by the spleen

Presentation

- failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable
- MCHC elevated

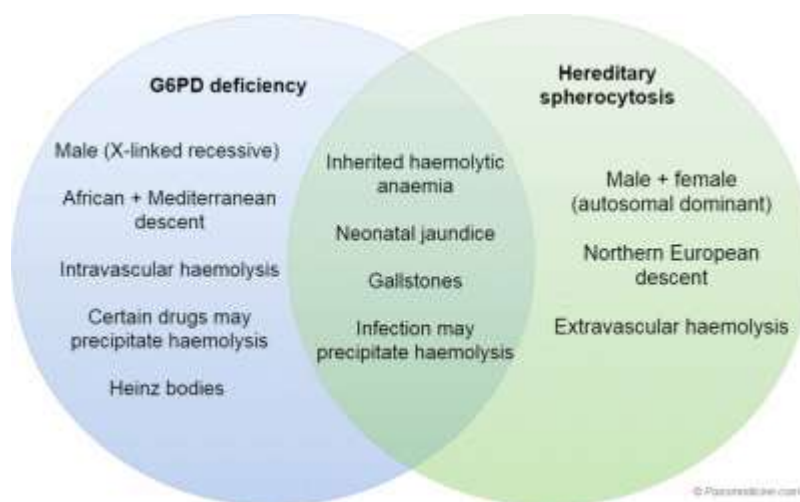
Diagnosis

- the osmotic fragility test was previously the recommended investigation of choice. However, it is now deemed unreliable and is no longer recommended
- the British Journal of Haematology (BJH) guidelines state that '*patients with a family history of HS, typical clinical features and laboratory investigations (spherocytes, raised mean corpuscular haemoglobin concentration [MCHC], increase in reticulocytes) do not require any additional tests*
- if the diagnosis is equivocal the BJH recommend the EMA binding test and the cryohaemolysis test
- for atypical presentations electrophoresis analysis of erythrocyte membranes is the method of choice

Management

- acute haemolytic crisis:
 - treatment is generally supportive
 - transfusion if necessary
- longer term treatment:
 - folate replacement
 - splenectomy

Comparing G6PD deficiency to hereditary spherocytosis:



	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent
Typical history	<ul style="list-style-type: none"> • Neonatal jaundice • Infection/drugs precipitate haemolysis • Gallstones 	<ul style="list-style-type: none"> • Neonatal jaundice • Chronic symptoms although haemolytic crises may be precipitated by infection • Gallstones • Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	EMA binding test



123


[Next question >](#)
B*I***A****T**

Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology



14



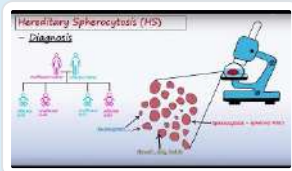
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[2011 Hereditary spherocytosis guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



Hereditary Spherocytosis (HS) - Pathophysiology

PhysioPathoPharmaco - YouTube



[Report broken media](#)

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A 35-year-old male Caucasian presents to the emergency department. He was asked to come to hospital after his GP noticed that his recent community blood tests showed severe anaemia. He attended his GP two days ago due to feeling increasingly tired and therefore the GP did routine blood tests for him. Apart from increasing fatigue and shortness of breath on exertion he had noticed nothing wrong. He had no past medical history apart from appendectomy when he was 20 years old and has recently significantly increased his exercise in an attempt to loose weight, and developed severe muscle aches, for which he has started to take diclofenac regularly. He denies any pain currently. On examination he is mildly jaundiced, has no stigmata of liver disease and his abdomen is soft without tenderness.

Blood tests:

Hb	96 g/l
Platelets	$357 \times 10^9/l$
WBC	$4.8 \times 10^9/l$
Blood film	spherocytosis
Na ⁺	138 mmol/l
K ⁺	4.9 mmol/l
Urea	4.7 mmol/l
Creatinine	79 μ mol/l
Bilirubin	58 μ mol/l
ALP	188 u/l
ALT	26 u/l

Further investigations are pending. What is the most likely diagnosis?

- ☐ G6PD deficiency ×
- ☐ Warm autoimmune haemolytic anaemia ×
- ☐ Peptic ulcer disease ×
- ☐ Sickle-cell anaemia ×
- ☐ Thalassaemia ×

Submit answer

Score: 0%

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Blood tests:

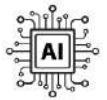
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Urea	4.7 mmol/l
Creatinine	79 µmol/l
Bilirubin	58 µmol/l
ALP	188 u/l
ALT	26 u/l

Further investigations are pending. What is the most likely diagnosis?

G6PD deficiency	34%
Warm autoimmune haemolytic anaemia	52%
Peptic ulcer disease	3%
Sickle-cell anaemia	5%
Thalassaemia	6%

Warm autoimmune haemolytic anaemia can be confirmed with the presence of anaemia, spherocytes on blood film and positive direct Coombs test for IgG or C3d

Important for me **Less important**



This is a patient who has developed symptomatic anaemia and jaundice following taking diclofenac, and has no symptoms of gastric irritation or signs of epigastric tenderness. Furthermore, the presence of elevated bilirubin suggests a haemolytic cause for the anaemia. These factors make peptic ulcer disease less likely.

Warm autoimmune haemolytic anaemia is the most likely explanation due to the evidence of haemolysis occurring following the administration of a drug known to cause this problem, and the presence of spherocytes supports this as well, but confirmation would be with a positive direct Coombs test.

G6PD deficiency is a cause for acute haemolytic anaemia but is more common in those of African ancestry and occurs typically after oxidating drugs such as primaquine.

Sickle-cell anaemia is very unlikely in a Caucasian patient and is also unlikely to be diagnosed at this age, and also would likely have a history of sickle-cell crisis.

Thalassemia is a disorder of globin genes causing ineffective erythropoiesis and haemolysis, endemic in the Mediterranean region and Africa. The blood film would be expected to show microcytosis and target cells rather than spherocytosis, and there is no evidence of extra-medullary haematopoiesis.



Discuss (10)

Improve

Next question >

Haemolytic anaemias: by site ★

In intravascular haemolysis, free haemoglobin is released which then binds to haptoglobin. As haptoglobin becomes saturated haemoglobin binds to albumin forming methaemalbumin (detected by Schumm's test). Free haemoglobin is excreted in the urine as haemoglobinuria, haemosiderinuria

Intravascular haemolysis: causes

- mismatched blood transfusion
- G6PD deficiency*
- red cell fragmentation: heart valves, TTP, DIC, HUS
- paroxysmal nocturnal haemoglobinuria

- cold autoimmune haemolytic anaemia

Extravascular haemolysis: causes

- haemoglobinopathies: sickle cell, thalassaemia
- hereditary spherocytosis
- haemolytic disease of newborn
- warm autoimmune haemolytic anaemia

*strictly speaking there is an element of extravascular haemolysis in G6PD as well, although it is usually classified as a intravascular cause



123



Next question >

B

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A

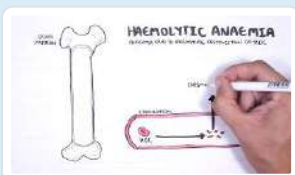


Textbooks

High-yield textbook

Extended textbook

Media



Haemolytic Anaemia - classification (intravascular, extravascular), pathophysiology, investigations

Armando Hasudungan - YouTube

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Question 51 of 191



A 65-year-old man attends the clinic with a three-month history of generalised, dull-aching bone pain and increased fatiguability. He has a history of hypertension, which is well-controlled with amlodipine 10 mg daily. On examination, he exhibits pallor and has bruises and petechiae on his shins and forearms. Laboratory results are attached.

Hb	7.6 g/L	Male: (135-180)
Platelets	39 * 10 ⁹ /L	(150 - 400)
WBC	3.1 * 10 ⁹ /L	(4.0 - 11.0)
Calcium	3.1 mmol/L	(2.1-2.6)
Creatinine	140 µmol/L	(55 - 120)

What is the most appropriate next investigation to determine the cause of this patient's bone pain?

- ☐ MRI spine ×
- ☐ Whole body MRI ×
- ☐ Whole body isotope bone scan ×
- ☐ Whole body low dose CT scan ×
- ☐ X-ray skull and spine ×

Submit answer

Reference ranges 

Score: **12%**

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A 65-year-old man attends the clinic with a three-month history of generalised, dull-aching bone pain and increased fatiguability. He has a history of hypertension, which is well-controlled with amlodipine 10 mg daily. On examination, he exhibits pallor and has bruises and petechiae on his shins and forearms. Laboratory results are attached.

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WBC	3.1 * 10 ⁹ /L	(4.0 - 11.0)
Calcium	3.1 mmol/L	(2.1-2.6)
Creatinine	140 µmol/L	(55 - 120)

What is the most appropriate next investigation to determine the cause of this patient's bone pain?

MRI spine	6%
Whole body MRI	64%
Whole body isotope bone scan	14%
Whole body low dose CT scan	5%
X-ray skull and spine	11%

Whole body MRI 1st line imaging in suspected multiple myeloma

Important for me Less important

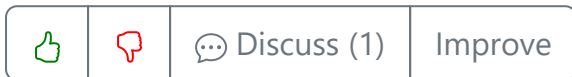
Whole body MRI is the preferred initial imaging modality for detecting myeloma-related bone disease and extra-medullary plasmacytomas. The clinical features of bone pain, fatigue, anaemia, thrombocytopenia, deranged creatinine, and hypercalcaemia in an older man are suggestive of multiple myeloma. It is standard practice to offer imaging to all patients with a suspected diagnosis of myeloma to investigate potential bone involvement, and a whole-body MRI is the most suitable investigation. This imaging modality can detect both lytic lesions and bone marrow infiltration, which are characteristic of multiple myeloma.

Whole body low dose CT scan is recommended as the first-line alternative for imaging in patients with myeloma in instances where an MRI is contraindicated due to the presence of a pacemaker, metallic heart valves, or aneurysm clips.

For comprehensive assessment in this context, a whole-body MRI would be necessary rather than just an **MRI spine**.

A **whole body isotope bone scan** is not indicated for initial screening of myeloma-related bone disease. An isotope bone scan relies on osteoblastic activity and may yield a false negative result, particularly in cases where bone turnover is not high.

An **x-ray skull** is not a primary imaging choice for evaluating myeloma-associated bone pathology. While a raindrop skull on an x-ray can support the diagnosis of multiple myeloma, it is not sensitive or specific enough to be used as a primary diagnostic tool.



Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
 - much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
 - this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor

- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

Clinical Knowledge Summaries



10



10

[Haematological cancers - recognition and referral](#)

NICE



12



6

Media



Multiple Myeloma - Diagnosis and Treatment

Medicosis Perfectionalis - YouTube

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Multiple Myeloma

Medicosis Perfectionalis - YouTube

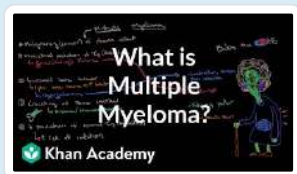
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Multiple Myeloma Mnemonic...the story of the plasma cell

Medicosis Perfectionalis - YouTube

👍 5 🗑️ 1



What is multiple myeloma?

Khan Academy - YouTube

👍 4 🗑️ 1



Multiple Myeloma

Townsend Teaching - YouTube

👍 3 🗑️ 1



Multiple Myeloma

CRASH! Medical Review - YouTube

👍 0 🗨️ 1



Multiple Myeloma

Armando Hasudungan - YouTube

👍 1 🗨️ 3

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Question 52 of 191



A 20-year-old female complains of feeling tired. She has no past medical history and takes no regular medications.

The following blood tests were obtained:

Hb	84g/L
MCV	70fL
WBC	$8 \times 10^9/L$
Platelets	$460 \times 10^9/L$

Blood film analysis comments on hypochromic anaemia with pencil cells, target cells, acanthocytes and Howell Jolly bodies.

What is the most likely diagnosis?

- ☐ Sickle cell anaemia ×
- ☐ Hereditary spherocytosis ×
- ☐ Thalassaemia trait ×
- ☐ Iron deficiency anaemia ×
- ☐ Coeliac disease ×

Submit answer

Reference ranges 

Score: 12%

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Blood film analysis comments on hypochromic anaemia with pencil cells, target cells, acanthocytes and Howell Jolly bodies.

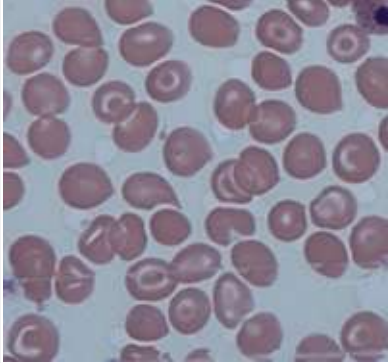
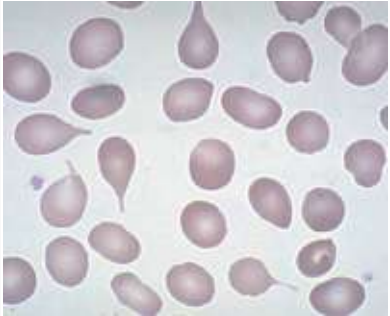
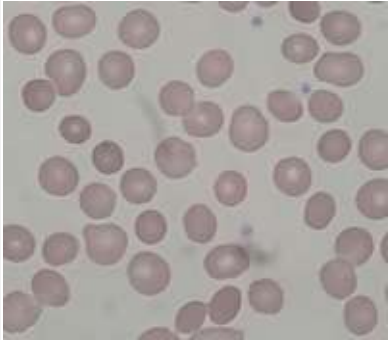
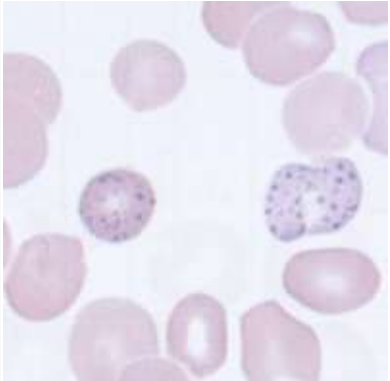
What is the most likely diagnosis?



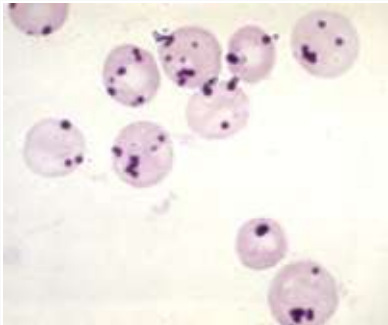
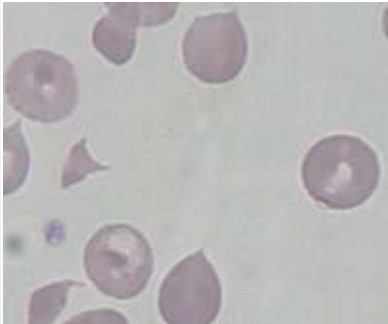
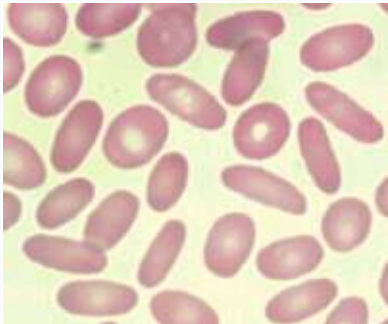
Sickle cell anaemia	10%
Hereditary spherocytosis	13%
Thalassaemia trait	20%
Iron deficiency anaemia	19%
Coeliac disease	37%


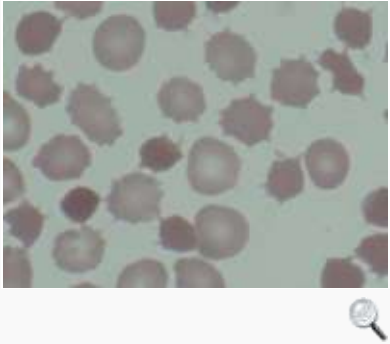
The blood film shows hypochromic anaemia with the presence of pencil cells that indicates the patient has iron deficiency anaemia. Target cells, acanthocytes and Howell Jolly bodies are features of hyposplenism. Iron deficiency and functional hyposplenism are both seen in coeliac disease, which is therefore the most likely unifying diagnosis. Thalassaemia trait is associated with mild reduction in haemoglobin, low MCV and low MCH; there would not be evidence of hyposplenism on the film in thalassaemia trait. Hereditary spherocytosis is due to a deficiency in spectrin, which leads to an abnormal red blood cell cytoskeleton. The film would show spherocytic red blood cells and reticulocytes. In sickle cell anaemia MCV is usually normal and sickle cells would be seen on the blood film.

Blood films: pathological cell forms ★

Pathological red cell forms

Abnormality	Associated condition(s)	Appearance
Target cells	Sickle-cell/thalassaemia Iron-deficiency anaemia Hyposplenism Liver disease	
'Tear-drop' poikilocytes	Myelofibrosis	
Spherocytes	Hereditary spherocytosis Autoimmune hemolytic anaemia	
Basophilic stippling	Lead poisoning Thalassaemia Sideroblastic anaemia Myelodysplasia	

Abnormality	Associated condition(s)	Appearance
		
Howell-Jolly bodies	Hyposplenism	
Heinz bodies	G6PD deficiency Alpha-thalassaemia	
Schistocytes ('helmet cells')	Intravascular haemolysis Mechanical heart valve Disseminated intravascular coagulation	
'Pencil' poikilocytes	Iron deficiency anaemia	

Abnormality	Associated condition(s)	Appearance
Burr cells (echinocytes)	Uraemia <u>Pyruvate kinase deficiency</u>	
Acanthocytes	<u>Abetalipoproteinemia</u>	

Other blood film abnormalities:

- hypersegmented neutrophils: megaloblastic anaemia


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123


Next question >

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Textbooks

High-yield textbook

Extended textbook

Score: **13.9%**

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| 1 | ✗ |
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91	×
92	×
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100	×
101	×
102	-



A 34-year-old man presents to the emergency department with abdominal pain. He has a background of multiple previous attendances with similar symptoms, which typically last for 3-7 days and then resolve. On a previous occasion, he underwent an exploratory laparoscopy, which did not identify a cause. He has a past medical history of depression. He takes citalopram. He does not smoke cigarettes or drink alcohol. He is a ceramicist. He has been under a lot of stress at work recently.

His observations are heart rate 111 beats per minute, blood pressure 153/74 mmHg, respiratory rate 18/minute, oxygen saturation 96% on room air and temperature 37°C.

Examination reveals a soft and non-tender abdomen with normal bowel sounds. There are no abnormalities of the external genitalia. A bilateral foot drop is noted on neurological examination.

Blood tests:

Hb	136 g/L	Male: (135-180) Female: (115 - 160)
Platelets	189 * 10 ⁹ /L	(150 - 400)
WBC	5.6 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	129 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	8.2 mmol/L	(2.0 - 7.0)
Creatinine	89 µmol/L	(55 - 120)
CRP	23 mg/L	(< 5)
Lactate	1.2 mmol/L	(0-2)

A urine sample is requested and it is noted to turn dark red when left standing.

Porphobilinogen is increased in the urine.

Plain radiography of the abdomen and chest are normal.

Based on the likely diagnosis, what is the most appropriate treatment?

☐ Chelation therapy



☐ IV hydrocortisone



<input type="radio"/> Supportive treatment only	×
<input type="radio"/> 5% dextrose	×
<input type="radio"/> Haem arginate and 10% dextrose	×

Submit answer

Reference ranges ▾

Score: 12%	
1	×
2	×
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4	×
5	✓
6	×
7	×
8	✓
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10	×
11	✓
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15	×
16	×
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22	×
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32	✓
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42	×
43	✓
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A urine sample is requested and it is noted to turn dark red when left standing.

Porphobilinogen is increased in the urine.

Plain radiography of the abdomen and chest are normal.

Based on the likely diagnosis, what is the most appropriate treatment?

- Chelation therapy

5%
- IV hydrocortisone

1%

Supportive treatment only

10%

5% dextrose

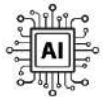
2%

Haem arginate and 10% dextrose

81%

IV haem arginate can be used to treat flares of acute intermittent porphyria

Important for me Less important



Haem arginate and 10% dextrose is the correct answer. This presents with features suggestive of acute intermittent porphyria (unexplained abdominal pain, depression, neuropathy, hyponatraemia, hypertension, tachycardia, red urine) and increased levels of urine porphobilinogen. Intravenous glucose inhibits the activity of aminolaevulinic acid synthase (an enzyme in the haem pathway). This reduces the overproduction of porphyrins. More hypotonic dextrose infusions should be avoided as they may worsen hyponatraemia. Haem arginate itself inhibits 5-aminolevulinic acid, which is another component in the porphyrin synthesis pathway. While the randomized control evidence of is lacking for this treatment, it is felt that patients typically respond well to this treatment and it should be given early in a severe attack.

5% dextrose is incorrect. Hypotonic dextrose solutions should be avoided as they may worsen hyponatraemia.

Chelation therapy is incorrect. Lead poisoning is a mimic of acute intermittent porphyria and can cause unexplained abdominal pain and neuropathy. However, the key distinction is that urine levels of porphobilinogen will not be increased in this condition. The diagnosis is typically confirmed by measuring levels of lead in the blood.

IV hydrocortisone is incorrect. Addison's disease can cause abdominal pain and hyponatraemia but you would expect hypotension rather than hypertension and the urinary findings are not typical of this condition.

Supportive treatment only is incorrect. This patient has a significant attack of acute intermittent porphyria with evidence of raised urinary porphobilinogen and motor neuropathy. This indicates a need for treatment with the above regimen.



Discuss (1)

Improve

Next question >

Acute intermittent porphyria ★

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40-year-olds. AIP is more common in females (5:1)

The classical presentation is a combination of abdominal, neurological and psychiatric symptoms:

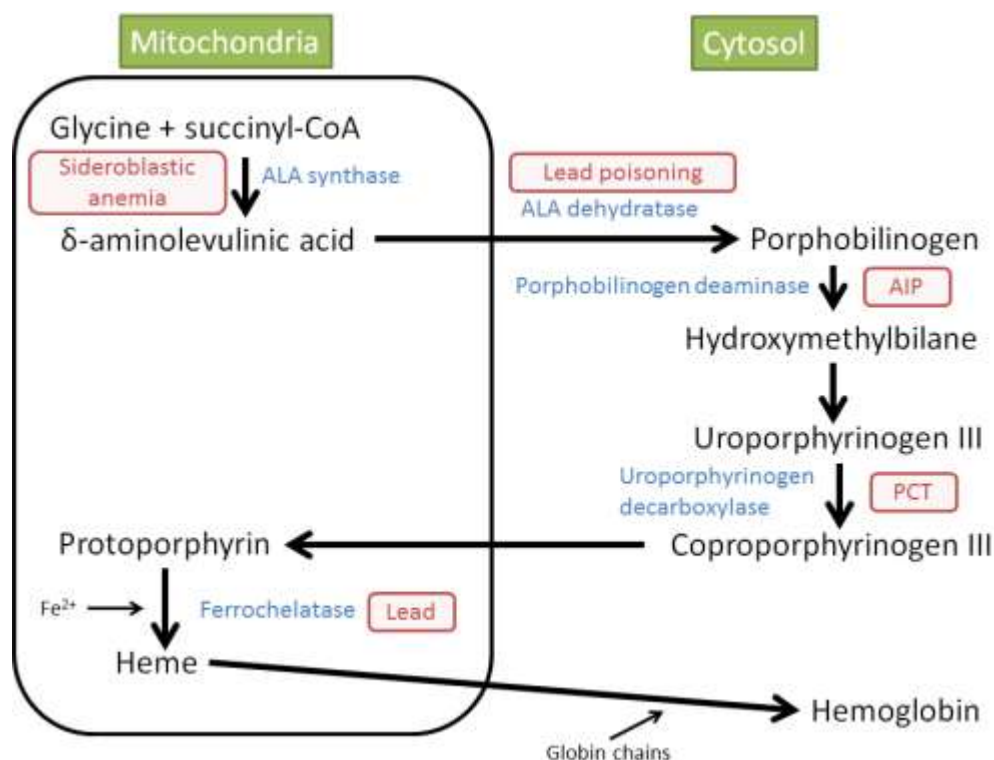
- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

Diagnosis

- classically urine turns deep red on standing
- raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
- assay of red cells for porphobilinogen deaminase
- raised serum levels of delta aminolaevulinic acid and porphobilinogen

Management

- avoiding triggers
- acute attacks
 - IV haematin/haem arginate
 - IV glucose should be used if haematin/haem arginate is not immediately available





123

[Next question >](#)**B***I***A****T**

Textbooks

[High-yield textbook](#)[Extended textbook](#)

Links

[Royal College of Physicians](#)

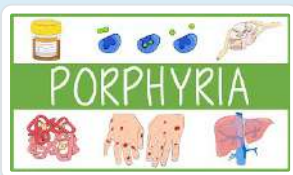
9



3

[2012 The acute porphyrias](#)[Suggest link](#)[Report broken link](#)

Media

[Porphyria](#)[Townsend Teaching - YouTube](#)

4



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[Acute intermittent porphyria](#)[Osmosis - YouTube](#)

17



3



Acute Intermittent Porphyria

Pixorize - YouTube

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[Report broken media](#)

Score: **13.9%**

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102 -



A 70-year-old man is referred to the haematology clinic by his general practitioner with anaemia. He has experienced progressive fatigue and shortness of breath for four months. On further questioning he also describes waking up at night soaked in sweat on one or two nights per week for the last month. His weight is stable. He has a past medical history of hypertension and COPD.

On examination he is pale. His heart sounds are normal and his chest is clear.. He has no ankle oedema and JVP is not raised. His abdomen is soft and he has splenomegaly 3cm below the costal margin with no hepatomegaly.

Test results sent with him by his GP are as follows:

Hb	92 g/l	Na ⁺	143 mmol/l
Platelets	143 * 10 ⁹ /l	K ⁺	3.7 mmol/l
WBC	4 * 10 ⁹ /l	Urea	7 mmol/l
Neuts	2 * 10 ⁹ /l	Creatinine	86 µmol/l
Lymphs	1 * 10 ⁹ /l	CRP	5 mg/l

Blood film: Anisocytosis with mild hypochromia. Tear drop cells. Mild thrombocytopenia with no platelet clumping.

Chest x-ray: Mildly hyperexpanded lung fields. No focal consolidation. No masses or lymphadenopathy.

Upper GI endoscopy & colonoscopy: Normal

Presence of which mutation is required to confirm the likely diagnosis?

- ☐ BCR-ABL ×
- ☐ BCL2 ×
- ☐ C-MYC ×
- ☐ JAK2 ×
- ☐ TP53 ×

Submit answer

Score: **12%**

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Blood film: Anisocytosis with mild hypochromia. Tear drop cells. Mild thrombocytopenia with no platelet clumping.

Chest x-ray: Mildly hyperexpanded lung fields. No focal consolidation. No masses or lymphadenopathy.

Upper GI endoscopy & colonoscopy: Normal

Presence of which mutation is required to confirm the likely diagnosis?

BCR-ABL	24%
BCL2	12%
C-MYC	15%
JAK2	40%
TP53	9%

This gentleman has B symptoms, anaemia and splenomegaly in the presence of characteristic tear

drops cells on the blood film, making myelofibrosis the most likely diagnosis. The British Committee for Standards in Haematology list several mutations which together with these symptoms and fibrosis on bone marrow form the diagnostic criteria. The most common of these is JAK2.

Presence of BCR-ABL is diagnostic for CML. BCL2 and TP53 mutations are seen in diffuse large B cell lymphoma.

C-MYC mutations are seen in Burkitt's lymphoma.

Use of JAK inhibitors in the management of myelofibrosis: a revision of the British Committee for Standards in Haematology Guidelines for Investigation and Management of Myelofibrosis 2012. British Journal of Haematology, 2014;;167;418438.

		 Discuss (5)	Improve
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Next question >

Myelofibrosis ★

Overview

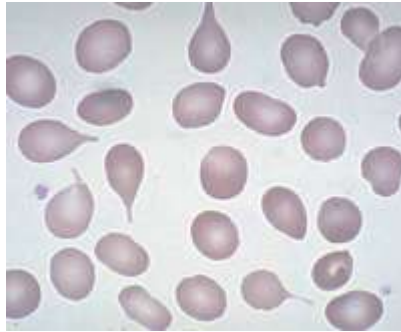
- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

Features

- e.g. elderly person with symptoms of anaemia e.g. fatigue (the most common presenting symptom)
- massive splenomegaly
- hypermetabolic symptoms: weight loss, night sweats etc

Laboratory findings

- anaemia
- high WBC and platelet count early in the disease
- 'tear-drop' poikilocytes on blood film
- unobtainable bone marrow biopsy - 'dry tap' therefore trephine biopsy needed
- high urate and LDH (reflect increased cell turnover)



Blood film showing the typical 'tear-drop' poikilocytes of myelofibrosis



123



Next question >

B

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A



T



Textbooks

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Links

British Journal of Haematology

0 1

[Use of JAK inhibitors in the management of myelofibrosis](#)

[Suggest link](#)

[Report broken link](#)

Media



[Myelofibrosis](#)

Osmosis - YouTube

👍 7 👎 0



Myelofibrosis

Medicosis Perfectionalis - YouTube 👍 3 👎 1



Myelofibrosis

Armando Hasudungan - YouTube 👍 5 👎 2

[Report broken media](#)

Score: **13.9%**

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93	✗
94	✓

95	×
96	×
97	×
98	×
99	×
100	×
101	×
102	-



A 48-year-old male with hepatitis C is admitted to the acute medical assessment unit having noticed a significant reduction in his urine output over the last few days. Urinalysis revealed haematoproteinuria, and his blood results are as follows:

Hb	9.8 g/dl
Platelets	$75 \times 10^9/l$
WBC	$12.1 \times 10^9/l$

Na ⁺	143 mmol/l
K ⁺	5.4 mmol/l
Urea	18.9 mmol/l
Creatinine	205 μ mol/l

A renal biopsy was subsequently performed and microscopy of the sample showed generally enlarged and hypercellular glomeruli with an increase in mesangial cellularity and matrix. A histological diagnosis of membranoproliferative glomerulonephritis is made. What is the most likely underlying pathology for this finding?

- ☐ Cryoglobulinaemia ×
- ☐ Haemolytic uraemic syndrome ×
- ☐ Hepato-renal syndrome ×
- ☐ Systemic lupus erythematosus ×
- ☐ Thrombotic thrombocytopenic purpura ×

Submit answer

Reference ranges 

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| 1 | ✗ |
| 2 | ✗ |
| 3 | ✗ |
| 4 | ✗ |
| 5 | ✓ |
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| 8 | ✓ |
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Cryoglobulinaemia

84%

Haemolytic uraemic syndrome

6%

Hepato-renal syndrome

3%

Systemic lupus erythematosus

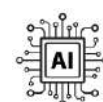
4%

Thrombotic thrombocytopenic purpura

3%

Hepatitis C is associated with mixed (type II) cryoglobulinaemia

Important for me Less important



This gentleman presents with acute kidney injury secondary to membranoproliferative glomerulonephritis. All of the listed options are recognised causes of membranoproliferative glomerulonephritis, but the key to this question is the patient's history of hepatitis C which is known to be closely associated with cryoglobulinaemia.

[Discuss \(7\)](#)[Improve](#)[Next question >](#)

Cryoglobulinaemia ★

Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C. One-third of cases are idiopathic

Three types

- type I (25%):
 - monoclonal - IgG or IgM
 - associations: multiple myeloma, Waldenstrom macroglobulinaemia
- type II (25%)
 - mixed monoclonal and polyclonal: usually with rheumatoid factor
 - associations: hepatitis C, rheumatoid arthritis, Sjogren's, lymphoma
- type III (50%)
 - polyclonal: usually with rheumatoid factor
 - associations: rheumatoid arthritis, Sjogren's

Possible features

- Raynaud's only seen in type I
- cutaneous
 - vascular purpura
 - distal ulceration
 - ulceration
- arthralgia
- renal involvement
 - diffuse glomerulonephritis

Investigations

- low complement (esp. C4)
- high ESR

Management

- treatment of underlying condition e.g. hepatitis C
- immunosuppression
- plasmapheresis



123



B


I



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Textbooks

High-yield textbook

Extended textbook

Score: **13.9%**

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92	✗
93	✗
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97	×
98	×
99	×
100	×
101	×
102	-



A 77-year-old man presents with a general decline in mobility, extreme lethargy, and weight loss.

His admission blood tests show:

Hb	98 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$119 \times 10^9/L$	(150 - 400)
WBC	$3.8 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	137 mmol/L	(135 - 145)
K ⁺	4.4 mmol/L	(3.5 - 5.0)
Urea	6.1 mmol/L	(2.0 - 7.0)
Creatinine	73 $\mu\text{mol/L}$	(55 - 120)
Calcium	2.46 mmol/L	(2.1-2.6)

A CT TAP is performed:

No evidence of solid organ malignancy or bony lesions. Splenomegaly noted - clinical correlation advised.

Given the ongoing concern for malignancy, a myeloma screen is sent:

IgA	0.56 g/L	(0.64-2.97)
IgG	4.7 g/L	(5.8-15.4)
IgM	12.52 g/L	(0.71-2.3)
Serum electrophoresis	Shows a paraprotein band	
Paraprotein level	44g/L	
Serum immunofixation	IgM type kappa paraprotein	
Serum free kappa light chains	13.65mg/L	(3.30-19.40)
Serum free lambda light chains	18.09 mg/L	(5.71-26.30)
Serum kappa / lambda ratio	0.75	(0.26-1.65)

What is the most likely diagnosis?

- ☐ Acute lymphoblastic leukaemia ×
- ☐ Monoclonal gammopathy of uncertain significance ×

- ☐ Multiple myeloma
- ☐ Smouldering myeloma
- ☐ Waldenstrom's macroglobulinaemia

Submit answer

Reference ranges ▾

Score: 12%	
1	×
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A 77-year-old man presents with a general decline in mobility, extreme lethargy, and weight loss.

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Serum free lambda light chains	18.09 mg/L	(5.71-26.30)
Serum kappa / lambda ratio	0.75	(0.26-1.65)

What is the most likely diagnosis?

- Acute lymphoblastic leukaemia
0%
- Monoclonal gammopathy of uncertain significance
17%

Multiple myeloma

8%

Smouldering myeloma

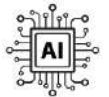
7%

Waldenstrom's macroglobulinaemia

68%

IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

Important for me **Less important**



Waldenstrom's macroglobulinaemia is the correct diagnosis. The patient presents with relatively non-specific symptoms; however, initial findings of pancytopenia and radiological evidence of splenomegaly are concerning for a haematological malignancy. Subsequent serological investigations revealing elevated serum free light chains and electrophoresis indicating a raised IgM level, alongside an IgM-type kappa paraprotein, strongly suggest Waldenstrom's macroglobulinaemia.


Acute lymphoblastic leukaemia (ALL) is not the appropriate diagnosis. ALL is characterised by the malignant proliferation of lymphoid progenitor cells and typically presents with lymphadenopathy and signs consistent with bone marrow infiltration by malignant clones, such as anaemia and thrombocytopenia. While initial blood tests may show leukocytosis, anaemia, and thrombocytopenia, elevated IgM levels (12.52 g/L) and an associated IgM-type kappa paraprotein indicate a monoclonal gammopathy rather than ALL. Lymphoid progenitor cells in ALL do not secrete immunoglobulins in large quantities; thus, the detection of a paraprotein band, specifically an IgM-type kappa paraprotein on serum electrophoresis, does not align with ALL but instead suggests plasma cell disorders such as Waldenstrom's macroglobulinaemia or multiple myeloma.

Monoclonal gammopathy of uncertain significance (MGUS) is also incorrect. Although MGUS with an IgM paraprotein could yield similar serum electrophoresis and immunofixation results to those observed in this case, MGUS is asymptomatic by definition—contrary to our patient who exhibits symptomatic anaemia. Furthermore, diagnostic criteria for MGUS stipulate that the paraprotein concentration must be below 30g/L; this patient's level exceeds this threshold at 44g/L. The combination of symptomatic presentation and a higher paraprotein level excludes MGUS as a diagnosis.

Multiple myeloma does not fit this clinical picture either. Defined by CRAB features (hypercalcaemia, renal failure, anaemia, bony lesions), multiple myeloma involves monoclonal plasma cell proliferation detectable via serum electrophoresis showing a paraprotein presence. However, an IgM-type kappa paraprotein is more indicative of Waldenstrom's macroglobulinaemia than multiple myeloma; the latter more commonly involves IgG or IgA production. Additionally, splenomegaly is less common in multiple myeloma cases. The absence of skeletal lesions further argues against multiple myeloma as a diagnosis here. While multiple myeloma can present with variable levels of serum free light chains depending on disease burden and subtype—a finding not

prominent in this patient—the normal range kappa/lambda ratio observed supports Waldenstrom's macroglobulinaemia over multiple myeloma.

Smouldering myeloma, like smouldering forms of other malignancies, presents without symptoms or end-organ damage—which includes CRAB features or any indication of organ impairment—and typically involves either IgG or IgA rather than IgM paraproteins. Given that our patient has symptomatic anaemia, smouldering myeloma is ruled out as a diagnosis in favour of Waldenstrom's macroglobulinaemia which accounts for both the symptomatology and laboratory findings observed.

   Discuss (3)  Improve

Next question >

Waldenstrom's macroglobulinaemia ★

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
 - the pentameric configuration of IgM increases serum viscosity
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Investigations







- **monoclonal IgM paraproteinaemia**
- bone marrow biopsy is diagnostic
 - infiltration of the bone marrow with lymphoplasmacytoid lymphoma cells

Management

- typically rituximab-based combination chemotherapy



Next question >

Textbooks



High-yield textbook

Extended textbook

Media





Waldenstrom's macroglobulinaemia

Medicosis Perfectionalis - YouTube  6  0





Waldenstrom's macroglobulinaemia

Osmosis - YouTube  5  0



What is Waldenstrom's macroglobulinaemia

Khan Academy Medicine - YouTube  0  0

[Report broken media](#)

Score: **13.9%**

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85	✓
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91	×
92	×
93	×
94	✓
95	×
96	×
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101	×
102	-



A 35-year-old patient with known sickle cell disease presents to the emergency department with new onset of left arm and facial weakness. The symptoms began earlier in the day. He is normally very careful with his sickle disease and ensures he is well hydrated and avoids the cold. His wife admits that over the last few days he has been suffering from nausea and vomiting and diarrhoea after he had a takeaway meal 3 days ago. On examination he his observations are within normal parameters. He has slurred speech and an obvious left facial droop with forehead sparing. He has power of 0/5 in his left arm but is otherwise neurologically intact.

His blood test show:

Hb	100 g/l
Platelets	$330 \times 10^9/l$
WBC	$8.9 \times 10^9/l$
INR	1.0

Na ⁺	138 mmol/l
K ⁺	3.5 mmol/l
Urea	9.9 mmol/l
Creatinine	135 μ mol/l
CRP	19 mg/L(<10)

Bilirubin	12 μ mol/l
ALP	89 u/l
ALT	39 u/l
Albumin	39 g/l

He is seen by the stroke team who arrange an urgent CT head which is reported as normal. What is the appropriate treatment for this gentleman?

- ☐ Thrombolysis ×
- ☐ Aspirin ×
- ☐ Plasmapheresis ×
- ☐ Methylprednisolone ×

☐ Exchange transfusion



Submit answer

Reference ranges

Score: **12%**

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| 11 | ✓ |
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57	-



Question 57 of 191



A 35-year-old patient with known sickle cell disease presents to the emergency department with new onset of left arm and facial weakness. The symptoms began earlier in the day. He is normally very careful with his sickle disease and ensures he is well hydrated and avoids the cold. His wife admits that over the last few days he has been suffering from nausea and vomiting and diarrhoea after he had a takeaway meal 3 days ago, On examination he his observations are within normal parameters. He has slurred speech and an obvious left facial droop with forehead sparing. He has power of 0/5 in his left arm but is otherwise neurologically intact.

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Urea	9.9 mmol/l
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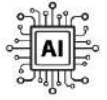
Bilirubin	12 µmol/l
ALP	89 u/l
ALT	39 u/l
Albumin	39 g/l

He is seen by the stroke team who arrange an urgent CT head which is reported as normal. What is the appropriate treatment for this gentleman?

Thrombolysis	7%
Aspirin	8%
Plasmapheresis	18%
Methylprednisolone	3%

Exchange transfusions are a way of reducing the number of sickle red cells and increasing the number of normal red cells, in order to improve oxygenation

Important for me **Less important**



This gentleman has a cerebral vaso-occlusive episode as a result of his sickle cell disease. The treatment of choice in these situations is urgent and aggressive exchange transfusion followed by transfusions to maintain HbS <30%. Thrombolysis and aspirin are not in the management guidelines for acute stroke in this situation.



Discuss (4)

Improve

Next question >

Sickle-cell crises: management ★

General management

- analgesia e.g. opiates
- rehydrate
- oxygen
- consider antibiotics if evidence of infection
- blood transfusion
 - indications include: severe or symptomatic anaemia, pregnancy, pre-operative
 - do not rapidly reduce the percentage of Hb S containing cells
- exchange transfusion
 - indications include: acute vaso-occlusive crisis (stroke, acute chest syndrome, multiorgan failure, splenic sequestration crisis)
 - rapidly reduce the percentage of Hb S containing cells



123



Next question >

B

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T





Textbooks

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Links

NICE

 3  4

[2012 Sickle cell disease: managing acute painful episodes in hospital](#)



[Suggest link](#)

[Report broken link](#)

Media













[Sickle cell anaemia](#)

Osmosis - YouTube  3  0

[Report broken media](#)

Score: **13.9%**

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94	✓
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Question 58 of 191



A 29-year-old man who is known to be HIV positive is reviewed. He has been taking anti-retroviral therapy for the past 2 years and has remained relatively well. Over the past few weeks however he has developed abdominal distension with some discomfort in the right iliac fossa. On examination a mass can be felt in the right lower quadrant. A biopsy shows a B cell lymphoma. Sheets of a medium sized lymphoid cells with high proliferative activity, forming a 'starry sky' appearance, are noted. What cytogenic abnormality is most likely to be found?

☐ t(11;14)



☐ t(14;18)



☐ t(8;14)



☐ t(9;22)





☐ t(11;18)



Submit answer

Reference ranges 

Score: 12%

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t(11;14)	11%
t(14;18)	17%
t(8;14)	57%
t(9;22)	12%
t(11;18)	4%

Burkitt's lymphoma - t(8;14)

Important for me Less important

This patient has an immunodeficiency-associated Burkitt lymphoma.

Discuss (2)

Improve

Next question >

Burkitt's lymphoma ★

Burkitt's lymphoma is a high-grade B-cell neoplasm. There are two major forms:

- endemic (African) form: typically involves maxilla or mandible
- sporadic form: abdominal (e.g. ileo-caecal) tumours are the most common form. More common in patients with HIV

Burkitt's lymphoma is associated with the c-myc gene translocation, usually t(8;14). The Epstein-Barr virus (EBV) is strongly implicated in the development of the African form of Burkitt's lymphoma and to a lesser extent the sporadic form.

Microscopy findings

- 'starry sky' appearance: lymphocyte sheets interspersed with macrophages containing dead apoptotic tumour cells

Management is with chemotherapy. This tends to produce a rapid response which may cause 'tumour lysis syndrome'. Rasburicase (a recombinant version of urate oxidase, an enzyme which catalyses the conversion of uric acid to allantoin*) is often given before the chemotherapy to reduce the risk of this occurring. Complications of tumour lysis syndrome include:

- hyperkalaemia
- hyperphosphataemia
- hypocalcaemia
- hyperuricaemia
- acute renal failure

*allantoin is 5-10 times more soluble than uric acid, so renal excretion is more effective



123



Next question >

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Media



Burkitt's Lymphoma

Medicosis Perfectionalis - YouTube

👍 7 👎 2



Burkitt's Lymphoma - Diagnosis and Treatment

Medicosis Perfectionalis - YouTube 👍 3 👎 1



Burkitt's lymphoma

Pixorize - YouTube 👍 3 👎 3

[Report broken media](#)

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Question 59 of 191



A 27-year-old woman is admitted after developing dyspnoea associated with pleuritic chest pain. A D-dimer taken on admission is elevated and subsequent CTPA shows a pulmonary embolism. Her past medical history includes a giving birth to her son 12 months ago (full term, vaginal delivery) and anxiety. She reports that her 47-year-old mother has had two deep vein thromboses in the past 10 years. Which one of the following is the most likely underlying cause?

- ☐ Factor V Leiden ×
- ☐ Antithrombin III deficiency ×
- ☐ Antiphospholipid syndrome ×
- ☐ Protein C deficiency ×
- ☐ Prothrombin gene mutation ×

Submit answer

Reference ranges 

Score: 12%

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Question 59 of 191

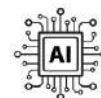


A 27-year-old woman is admitted after developing dyspnoea associated with pleuritic chest pain. A D-dimer taken on admission is elevated and subsequent CTPA shows a pulmonary embolism. Her past medical history includes a giving birth to her son 12 months ago (full term, vaginal delivery) and anxiety. She reports that her 47-year-old mother has had two deep vein thromboses in the past 10 years. Which one of the following is the most likely underlying cause?

Factor V Leiden	70%
Antithrombin III deficiency	8%
Antiphospholipid syndrome	10%
Protein C deficiency	10%
Prothrombin gene mutation	1%

Activated protein C resistance (Factor V Leiden) is the most common inherited thrombophilia

Important for me Less important



NICE would recommend testing for thrombophilia given the unprovoked venous thromboembolism and family history.




 Discuss (4)

 Improve

Next question >

Thrombophilia: causes ★

Inherited

Gain of function polymorphisms

- factor V Leiden (activated protein C resistance): most common cause of thrombophilia
- prothrombin gene mutation: second most common cause

Deficiencies of naturally occurring anticoagulants

- antithrombin III deficiency
- protein C deficiency
- protein S deficiency

The table below shows the prevalence and relative risk of venous thromboembolism (VTE) of the different inherited thrombophilias:

Condition	Prevalence	Relative risk of VTE
Factor V Leiden (heterozygous)	5%	4
Factor V Leiden (homozygous)	0.05%	10
Prothrombin gene mutation (heterozygous)	1.5%	3
Protein C deficiency	0.3%	10
Protein S deficiency	0.1%	5-10
Antithrombin III deficiency	0.02%	10-20

Acquired

Antiphospholipid syndrome

Drugs

- the combined oral contraceptive pill



+

Q

123



Next question >

B

I



A



T



Textbooks

High-yield textbook

Extended textbook

Links

Rare Disease Video Library - NORD

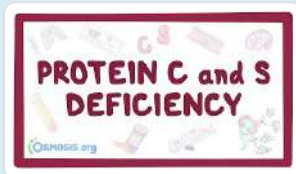
👍 5 👎 3

[Protein C and Protein S Deficiency](#)

[Suggest link](#)

[Report broken link](#)

Media



[Protein C and S deficiency](#)

Osmosis - YouTube 👍 4 👎 1

[Report broken media](#)

Score: **13.9%**

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Question 60 of 191



A 19-year-old man with hereditary spherocytosis is reviewed in the clinic. He was last admitted to the hospital some 6 months earlier for an acute haemolytic crisis related to parvovirus infection. He complains that he feels chronically tired and has persistent left upper quadrant pain and discomfort. Abdominal examination confirms splenomegaly.

Investigations:

Abdominal ultrasound scan reveals splenomegaly and a solitary gallstone visualised within the gallbladder.

Hb	90 g/l
MCV	101 fL
Platelets	$301 \times 10^9/l$
WBC	$7.1 \times 10^9/l$

Which of the following is the most appropriate intervention for him?

- ☐ Prednisolone ×
- ☐ Splenectomy ×
- ☐ Cholecystectomy ×
- ☐ Oral iron supplementation ×
- ☐ IV iron supplementation ×

Submit answer

Reference ranges 

Score: 12%

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A 19-year-old man with hereditary spherocytosis is reviewed in the clinic. He was last admitted to the hospital some 6 months earlier for an acute haemolytic crisis related to parvovirus infection. He complains that he feels chronically tired and has persistent left upper quadrant pain and discomfort. Abdominal examination confirms splenomegaly.

Investigations:

Abdominal ultrasound scan reveals splenomegaly and a solitary gallstone visualised within the gallbladder.

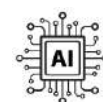
Hb	90 g/l
MCV	101 fL
Platelets	$301 \times 10^9/l$
WBC	$7.1 \times 10^9/l$

Which of the following is the most appropriate intervention for him?

Prednisolone	8%
Splenectomy	79%
Cholecystectomy	9%
Oral iron supplementation	3%
IV iron supplementation	2%

Elective splenectomy is appropriate in a patient with hereditary spherocytosis who has recurrent anaemia

Important for me Less important



This patient has hereditary spherocytosis with evidence of chronic haemolysis. Although this patient doesn't yet have symptoms of cholecystitis they have evidence of possible pigment gallstone formation on the ultrasound scan and symptomatic splenomegaly. Coupled with the anaemia and raised MCV (suggestive of increased reticulocytes), this clinical picture points to elective splenectomy as the most appropriate option, with vaccination at least against

pneumococcus before the procedure is carried out.

Cholecystectomy is carried out where patients present with cholecystitis related to hereditary spherocytosis. Prednisolone may help stimulate red cell production in situations where there is an acute haemolytic crisis. There is no role for iron supplementation here. IV iron supplementation is usually considered for patients with chronic renal impairment.

		 Discuss (4)	Improve
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Next question >

Hereditary spherocytosis ★

Basics

- most common hereditary haemolytic anaemia in people of northern European descent
- autosomal dominant defect of red blood cell cytoskeleton
- the normal biconcave disc shape is replaced by a sphere-shaped red blood cell
- red blood cell survival reduced as destroyed by the spleen

Presentation

- failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable
- MCHC elevated

Diagnosis

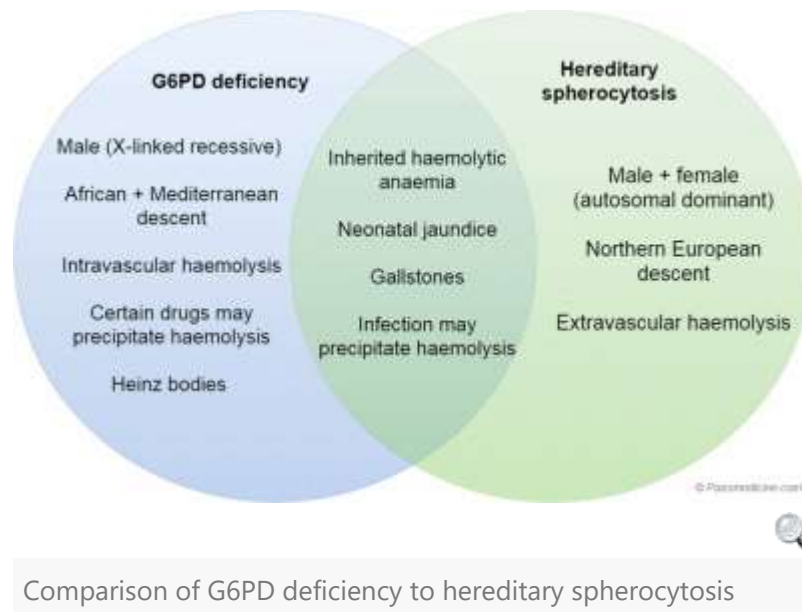
- the osmotic fragility test was previously the recommended investigation of choice. However, it is now deemed unreliable and is no longer recommended
- the British Journal of Haematology (BJH) guidelines state that '*patients with a family history of HS, typical clinical features and laboratory investigations (spherocytes, raised mean corpuscular haemoglobin concentration [MCHC], increase in reticulocytes) do not require any additional tests*
- if the diagnosis is equivocal the BJH recommend the EMA binding test and the cryohaemolysis test
- for atypical presentations electrophoresis analysis of erythrocyte membranes is the method of choice

Management

- acute haemolytic crisis:
 - treatment is generally supportive

- transfusion if necessary
- longer term treatment:
 - folate replacement
 - splenectomy

Comparing G6PD deficiency to hereditary spherocytosis:



	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent
Typical history	<ul style="list-style-type: none"> • Neonatal jaundice • Infection/drugs precipitate haemolysis • Gallstones 	<ul style="list-style-type: none"> • Neonatal jaundice • Chronic symptoms although haemolytic crises may be precipitated by infection • Gallstones • Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	EMA binding test

Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

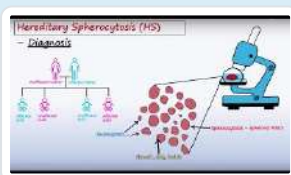
👍 14 👎 7

[2011 Hereditary spherocytosis guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Hereditary Spherocytosis \(HS\) - Pathophysiology](#)

PhysioPathoPharmaco - YouTube 👍 3 👎 0

[Report broken media](#)

Score: **13.9%**

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Question 61 of 191



A 60-year-old woman presents to the clinic with a one-year history of generalised body pain and fatigue. She intermittently experiences epistaxis and bleeding gums. She underwent a fundoscopy for blurred vision, which showed retinal haemorrhages and dilated retinal veins. Examination reveals pallor and hepatosplenomegaly. Serum protein electrophoresis demonstrates a sharp, narrow spike of monoclonal IgM. A skeletal survey is normal. A bone marrow biopsy is scheduled.

What are the expected findings of the bone marrow biopsy for this patient?

- ☐ <10% infiltration of bone marrow with lymphoplasmacytic cells ×
- ☐ <10% monoclonal plasma cells ×
- ☐ >10% infiltration of bone marrow with lymphoplasmacytic cells ×
- ☐ >10% monoclonal plasma cells with clock-face chromatin ×
- ☐ Abnormal B cells ×

Submit answer

Reference ranges 

Score: 12%

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- 9 ×

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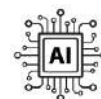
A 60-year-old woman presents to the clinic with a one-year history of generalised body pain and fatigue. She intermittently experiences epistaxis and bleeding gums. She underwent a fundoscopy for blurred vision, which showed retinal haemorrhages and dilated retinal veins. Examination reveals pallor and hepatosplenomegaly. Serum protein electrophoresis demonstrates a sharp, narrow spike of monoclonal IgM. A skeletal survey is normal. A bone marrow biopsy is scheduled.

What are the expected findings of the bone marrow biopsy for this patient?

<10% infiltration of bone marrow with lymphoplasmacytic cells	15%
<10% monoclonal plasma cells	16%
> 10% infiltration of bone marrow with lymphoplasmacytic cells	51%
> 10% monoclonal plasma cells with clock-face chromatin	17%
Abnormal B cells	2%

IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

Important for me Less important




> 10% infiltration of the bone marrow with lymphoplasmacytic cells is the typical bone marrow finding observed in patients with Waldenstrom's macroglobulinemia, which is the case here. The patient's presentation and investigations are consistent with Waldenstrom's macroglobulinaemia, a lymphoplasmacytic malignancy characterised by the secretion of a monoclonal IgM paraprotein. The disease typically presents with systemic symptoms such as fatigue and weight loss, hyperviscosity syndrome (e.g., blurred vision due to retinal haemorrhages), and hepatosplenomegaly.

< 10% infiltration of bone marrow with lymphoplasmacytic cells is typically observed in monoclonal gammopathy of undetermined significance (MGUS). The features such as anaemia, hepatosplenomegaly and hyperviscosity symptoms outlined in this scenario are rarely associated with MGUS; hence, this option is not applicable.

< 10% monoclonal plasma cells is incorrect because it is < 10% monoclonal plasma cells can be seen in MGUS.

It is important to distinguish this condition from multiple myeloma. The lack of bony lesions and normal skeletal survey findings exclude multiple myeloma in this case. Additionally, IgM myeloma is exceedingly uncommon. > **10% monoclonal plasma cells with clock-face chromatin** typify multiple myeloma; therefore this choice is incorrect.

Chronic lymphocytic leukaemia (CLL) represents another differential diagnosis characterised by **abnormal B cells** within the bone marrow. Monoclonal gammopathy is uncommon in CLL. Serum protein electrophoresis typically appears normal in CLL cases and only demonstrates abnormal protein spikes in approximately 15% of instances.

   Discuss (1)  Improve

Next question >

Waldenstrom's macroglobulinaemia ★

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
 - the pentameric configuration of IgM increases serum viscosity
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Investigations









- **monoclonal IgM paraproteinaemia**
- bone marrow biopsy is diagnostic
 - infiltration of the bone marrow with lymphoplasmacytoid lymphoma cells

Management

- typically rituximab-based combination chemotherapy



Next question >

Textbooks



High-yield textbook

Extended textbook

Media





Waldenstrom's macroglobulinaemia

Medicosis Perfectionalis - YouTube  6  0





Waldenstrom's macroglobulinaemia

Osmosis - YouTube  5  0



What is Waldenstrom's macroglobulinaemia

Khan Academy Medicine - YouTube  0  0

[Report broken media](#)

Score: **13.9%**

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Question 62 of 191



A 28-year-old Afro-Caribbean male presents with a two-hour history of sudden onset left sided weakness. He denies any sensory involvement, dysarthria or dysphasia. He has a known history of sickle cell disease, with two previous episodes of transient ischaemic attacks and an episode of acute chest syndrome attack 10 days ago. On examination, he displays power of 1/5 in his left arm, 2/5 in his left leg, 5/5 in his right side. He reports no sensory disturbances, plantar responses are downgoing bilaterally, he is unable to perform finger-nose testing. He denies any illicit drug use, is a non-smoker and does not drink alcohol. He has no other past medical history. A hyperacute CT head demonstrates an area of acute ischaemia in the right internal capsule region. What is the most appropriate immediate treatment?

- ☐ Intravenous thrombolysis ×
- ☐ Aspirin 300mg ×
- ☐ Intravenous thrombolysis and mechanical thrombectomy ×
- ☐ Exchange transfusion ×
- ☐ Clopidogrel 300mg ×

Submit answer

Reference ranges 

Score: **12%**

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Question 62 of 191

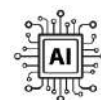


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Intravenous thrombolysis	8%
Aspirin 300mg	8%
Intravenous thrombolysis and mechanical thrombectomy	16%
Exchange transfusion	67%
Clopidogrel 300mg	1%


Exchange transfusions are a way of reducing the number of sickle red cells and increasing the number of normal red cells, in order to improve oxygenation


Important for me [Less important](#)



This patient has presented with an acute vaso-occlusive crisis on a background of known sickle cell disease. He is at high risk of an infarctive stroke given the background of previous TIAs (increased relative risk by 56 times) and a recent chest crisis within the past 2 weeks (increased relative risk by 7 times). The other risk factors include a high systolic pressure (RR 1.3 increase per 10mmHg) and a low steady state haemoglobin (RR 1.9 per 1g/dL decrease)¹. The management of an acute sickle infarct is different to that of thromboembolic stroke or atheromatous disease. The immediate aim is to reduce the proportion of HbS, either with immediate transfusion or optimally, with exchange transfusion. The latter reduces the concentration of HbS faster with a lower risk of transfusional volume overload, possibly resulting in increased blood viscosity and consequent pulmonary oedema.

1. Ohene-Frempong K, Weiner SJ, Sleeper LA et al. Cerebrovascular accidents in sickle cell disease:





Discuss (3)

Improve

Next question >






Sickle-cell crises: management ★

General management

- analgesia e.g. opiates
- rehydrate
- oxygen
- consider antibiotics if evidence of infection
- blood transfusion
 - indications include: severe or symptomatic anaemia, pregnancy, pre-operative
 - do not rapidly reduce the percentage of Hb S containing cells
- exchange transfusion
 - indications include: acute vaso-occlusive crisis (stroke, acute chest syndrome, multiorgan failure, splenic sequestration crisis
 - rapidly reduce the percentage of Hb S containing cells



Next question >

B *I*  **A** ▼    ▼ **T** ▼  ▼  



Textbooks

High-yield textbook

Extended textbook

Links

NICE

 3  4

2012 Sickle cell disease: managing acute painful episodes in hospital



[Suggest link](#)

[Report broken link](#)

Media



[Sickle cell anaemia](#)

Osmosis - YouTube  3  0

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Score: **13.9%**

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92	✗
93	✗
94	✓
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96	×
97	×
98	×
99	×
100	×
101	×
102	-



A 25 year old man presented to the Emergency Department with acute onset, rapidly progressive weakness in all the four limbs following a bout of severe colicky abdominal pain which lasted for 10 days but eventually subsided. The abdominal pain was located around the umbilicus, stabbing in nature, radiated towards the back, and was associated with nausea and intermittent constipation. Patient reports weakness originating in both arms then affecting both the lower limbs. He also complains of difficulty in closing his lips and eyes, and has uncontrolled salivation from the angles of the mouth. He denied any history of paraesthesia, sphincteric disturbances, epileptic fits or dark colored urine during any of the episodes. No definite history of any drug intake prior to both the episodes could be ascertained.

Physical examination revealed bilateral facial palsy of lower motor neuron (LMN) type together with flaccid quadriparesis which was more marked distally with bilateral wrist drop. Deep tendon reflexes were diminished in both upper and lower limbs. There was no sensory loss.

Initial lab values showed WBCs $8.9 \times 10^9/L$, Hemoglobin of 12g/L, Sodium of 132mmol/L, and ESR of 35mm/Hr. His temperature was 36.5 C and pulse 83/min. His blood pressure was 130/83 mm/Hg and oxygen saturations were 98% on air. A lumbar puncture was performed and CSF studies were normal.

Which of the following is most likely to be diagnostic?

- | | |
|--|---|
| <input type="radio"/> CT scan with contrast of abdomen | × |
| <input type="radio"/> MRI brain with contrast | × |
| <input type="radio"/> Urine screen for Vanillylmandelic acid (VMA) | × |
| <input type="radio"/> Urine screen for Aminolevulinic Acid (ALA) and Porphobilinogen (PBG) | × |
| <input type="radio"/> Measurement of urinary and stool porphyrins | × |

Submit answer

Reference ranges 

- | | |
|----|---|
| 1 | ✗ |
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48	×
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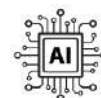
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Which of the following is most likely to be diagnostic?

CT scan with contrast of abdomen	2%
MRI brain with contrast	3%
Urine screen for Vanillylmandelic acid (VMA)	8%
Urine screen for Aminolevulinic Acid (ALA) and Porphobilinogen (PBG)	75%
Measurement of urinary and stool porphyrins	12%

In acute intermittent porphyria, urinary porphobilinogen is typically raised

Important for me Less important




Acute attacks of Acute Intermittent Porphyria (AIP) are often precipitated by drugs like barbiturates, sulfonamides, chloroquin, griseofulvin, diphenyl hydantoin and many other drugs, acute infections and over-indulgence in alcohol. Acute attacks are due to greatly increased activity

of delta-aminolaevulinic acid synthetase. During acute attacks, the urine contains large amounts of porphobilinogen (PBG) and delta-aminolaevulinic acid (ALA) which, on standing, gives dark 'port-wine' colour to the urine. Mental disturbances during acute episodes are of metabolic origin while neurological weakness of the extremities is due to focal demyelination and/or axonal degeneration of peripheral and autonomic nerves.

Onset of symptoms usually occurs in adolescence. Females are more commonly affected than males. The clinical picture is dominated by gastrointestinal and neurological manifestations. Symptoms during acute episodes usually comprise of severe colicky pain in the abdomen which may be diffuse or localized-usually to the umbilical or epigastric region and is often associated with nausea and vomiting and occasionally diarrhea. Diagnosis in such patients may be missed, unduly delayed or confused with acute surgical abdomen especially if neurological manifestations are lacking. Gastrointestinal manifestations are related to severe intestinal spasm due to autonomic dysfunction. Neurological manifestations comprise of flaccid paralysis, neuropsychiatric disturbances and rarely generalized epileptic fits. Paralysis may be confined to lower or upper extremities or may affect all the four limbs. It may be more marked proximally or distally or may be generalized and is due to predominant motor neuropathy. Sensory symptoms may also occur but objective sensory loss is unusual. Epileptic fits in AIP have been reported in about 15 to 20% cases. Bulbar paralysis and respiratory involvement can also occur and may threaten the life of the patient. Sphincteric disturbances are uncommon. Skin lesions are seldom seen.

Diagnosis of AIP should be suspected in any patient presenting with rapidly progressive flaccid paralysis with severe abdominal pain and history of passing dark reddish urine. Examination of the urine during acute attacks for PBG and ALA will help in establishing the diagnosis. In the patient in the above case, the diagnosis of AIP was based on clinical and urinary findings.

There is no specific treatment for porphyria and it is therefore very important to prevent the onset of acute attack. Treatment during acute episodes usually comprises symptomatic and general supportive measures for bulbar and respiratory paralysis, if it occurs. Chlorpromazine has been reported to be beneficial in relieving pain and other symptoms. Approximately 25% siblings of patients of AIP may be expected to have PBG in urine and therefore screening of siblings and other family members should be done. Prophylaxis in such cases as well as those known to clinically manifest AIP includes the avoidance of drugs known to precipitate the acute attacks as enlisted above.

		 Discuss (11)	Improve
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Next question >

Acute intermittent porphyria ★

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents

with abdominal and neuropsychiatric symptoms in 20-40-year-olds. AIP is more common in females (5:1)

The classical presentation is a combination of abdominal, neurological and psychiatric symptoms:

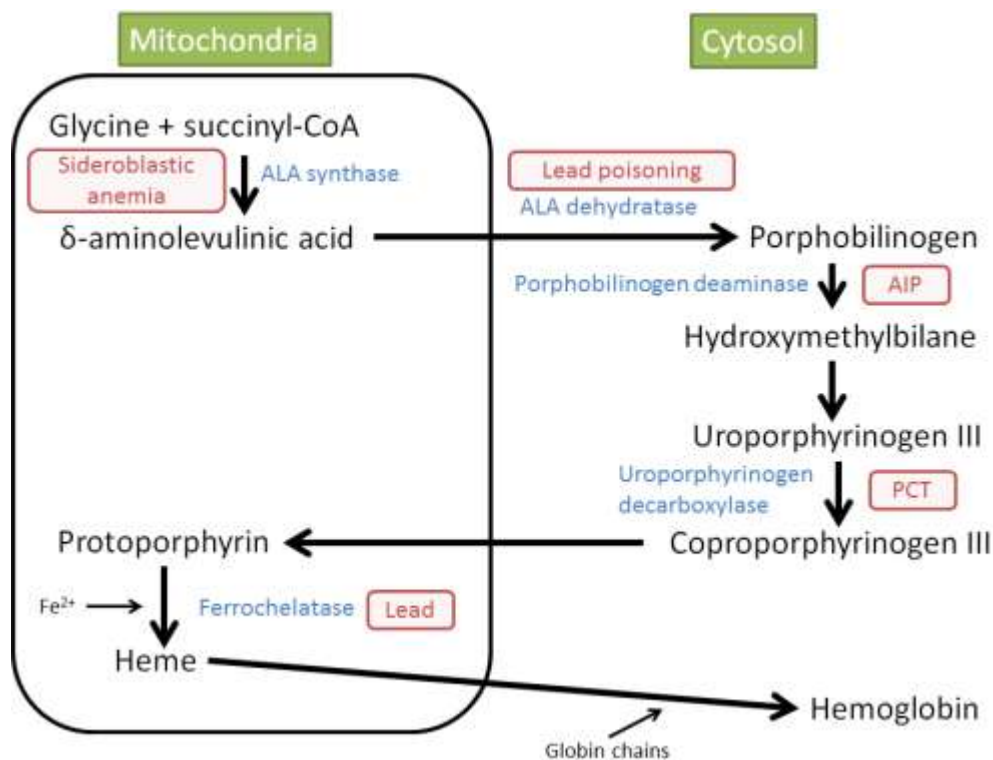
- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

Diagnosis

- classically urine turns deep red on standing
- raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
- assay of red cells for porphobilinogen deaminase
- raised serum levels of delta aminolaevulinic acid and porphobilinogen

Management

- avoiding triggers
- acute attacks
 - IV haematin/haem arginate
 - IV glucose should be used if haematin/haem arginate is not immediately available



Textbooks

High-yield textbook

Extended textbook

Links

Royal College of Physicians

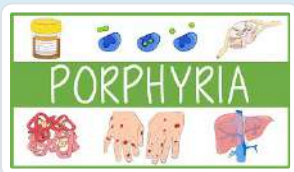
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[2012 The acute porphyrias](#)



[Suggest link](#)

[Report broken link](#)

Media





[Porphyria](#)

Townsend Teaching - YouTube  4  0



[Acute intermittent porphyria](#)

Osmosis - YouTube  17  3



[Acute Intermittent Porphyria](#)



Score: **13.9%**

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101	✗
102	-



A 55-year-old man is referred by her GP to the haematology clinic. He reports a four-week history of night sweats and early satiety. On questioning, he elaborates and says that he has been feeling unwell for some time, but that he had just started work as a managing director and had attributed this to the added stress of his promotion.

On examination, he is pale with an unremarkable cardiovascular and respiratory exam. There is a fullness in the left upper quadrant which moves with inspiration and widespread small volume lymphadenopathy.

His blood tests are shown below:

Hb	100 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$117 \times 10^9/L$	(150 - 400)
WBC	$30.1 \times 10^9/L$	(4.0 - 11.0)
Neuts	$4.0 \times 10^9/L$	(2.0 - 7.0)
Lymphs	$25.0 \times 10^9/L$	(1.0 - 3.5)
Mono	$0.8 \times 10^9/L$	(0.2 - 0.8)
Eosin	$0.3 \times 10^9/L$	(0.0 - 0.4)
Blood Film	lymphocytosis with smudge cells	

A bone marrow biopsy shows lymphocytosis in a diffuse growth pattern.

Chromosomal analysis is performed to guide further management.

Given the likely diagnosis, which of the following findings would suggest a poor prognosis?

- ☐ Wild-type TP53 ×
- ☐ >2% mutated immunoglobulin heavy chain variable region ×
- ☐ Deletion of 13q ×
- ☐ Mutated TP53 ×
- ☐ < 20% expression of CD38 lymphocytes ×

Submit answer

Score: **12%**

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| 1 | ✗ |
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64	-

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Lymphs	25.0 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.8 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.3 * 10 ⁹ /L	(0.0 - 0.4)
Blood Film	lymphocytosis with smudge cells	

A bone marrow biopsy shows lymphocytosis in a diffuse growth pattern.

Chromosomal analysis is performed to guide further management.

Given the likely diagnosis, which of the following findings would suggest a poor prognosis?

Wild-type TP53	10%
>2% mutated immunoglobulin heavy chain variable region	4%
Deletion of 13q	25%
Mutated TP53	54%
< 20% expression of CD38 lymphocytes	6%

TP53 mutation is associated with a poor prognosis in CLL

This patient has aggressive chronic lymphocytic leukaemia (CLL) with both constitutional symptoms and bone marrow failure, indicating the need for treatment. The chromosomal analysis may be used to guide treatment offers significant insights into prognostication.

The presence of a mutated TP53 is a poor prognostic marker, where a 'wild type' refers to an unmutated form and is a good prognostic marker. A >2% mutated immunoglobulin heavy chain variable region, deletion of 13q or < 20% expression of CD38 lymphocytes are good prognostic markers.



Discuss (3)

Improve

Next question >

Chronic lymphocytic leukaemia: prognostic factors ★

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive
- TP53 mutation

Chromosomal changes

- deletion of the long arm of chromosome 13 (del 13q) is the most common abnormality, being seen in around 50% of patients. It is associated with a **good** prognosis
- deletions of part of the short arm of chromosome 17 (del 17p) are seen in around 5-10% of patients and are associated with a **poor** prognosis



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

👍 5 👎 1

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)

Medicosis Perfectionalis - YouTube

👍 3 👎 0

[Report broken media](#)

Score: **13.9%**

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100	×
101	×
102	-



A 26-year-old gentleman presents to haematology clinic one week prior to starting chemotherapy for acute myeloid leukaemia (AML). He is currently feeling fatigued, suffering from night sweats, and has chronic lower back pain. He is anxious to start treatment. His past medical history includes ankylosing spondylitis and a clavicular fracture. His current medications include paracetamol and ibuprofen.

Blood tests:

Hb	113 g/l
Platelets	156 * 10 ⁹ /l
WBC	57 * 10 ⁹ /l
Na ⁺	140 mmol/l
K ⁺	3.6 mmol/l
Urea	4.2 mmol/l
Creatinine	63 µmol/l

What measure is the least useful to prevent tumour lysis syndrome?

- ☐ IV fluids prior to chemotherapy ×
- ☐ Urine alkalization ×
- ☐ Prophylactic allopurinol ×
- ☐ Prophylactic rasburicase ×
- ☐ Stopping NSAID use ×

Submit answer

Reference ranges 

Score: 12%

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Urea	4.2 mmol/l
Creatinine	63 µmol/l

What measure is the least useful to prevent tumour lysis syndrome?

IV fluids prior to chemotherapy	9%
Urine alkalization	34%
Prophylactic allopurinol	15%
Prophylactic rasburicase	15%
Stopping NSAID use	27%

This patient has AML with a high white cell count and is about to start chemotherapy, and is therefore at high risk of tumour lysis syndrome (TLS). The key is to prevent TLS, which is done by ensuring good renal perfusion. Commonly this can be done by aggressive intravenous hydration prior to the start of treatment and stop NSAIDs, such as ibuprofen for this patient. Allopurinol and rasburicase both prevent uric acid accumulation and can, therefore, be used as well. Urine alkalization has not shown to be effective.

Source:

Larson, Richard A., and Ching-Hon Pui. 'Tumor Lysis Syndrome: Prevention and Treatment.' UpToDate. N.p., 4 Oct. 2016.

[Discuss \(5\)](#)[Improve](#)[Next question >](#)

Tumour lysis syndrome ★

Tumour lysis syndrome (TLS) is a potentially deadly condition related to the treatment of high-grade lymphomas and leukaemias. It can occur in the absence of chemotherapy but is usually triggered by the introduction of combination chemotherapy. On occasion, it can occur with steroid treatment alone. Awareness of the condition is critical as prophylactic medication can be given to prevent the potentially deadly effects of tumour cell lysis.

TLS occurs from the breakdown of the tumour cells and the subsequent release of chemicals from the cell. It leads to a high potassium and high phosphate level in the presence of a low calcium. It should be suspected in any patient presenting with an acute kidney injury in the presence of a high phosphate and high uric acid level.

Prevention

- IV fluids
- patients at higher risk should receive either allopurinol or rasburicase
- rasburicase
 - a recombinant version of urate oxidase, an enzyme that metabolizes uric acid to allantoin. Allantoin is much more water-soluble than uric acid and is, therefore, more easily excreted by the kidneys
 - generally preferred now for patients at a higher risk of developing TLS
- allopurinol
 - generally used for patients in lower-risk groups
- rasburicase and allopurinol should not be given together in the management of tumour lysis syndrome as this reduces the effect of rasburicase

From 2004 TLS has been graded using the Cairo-Bishop scoring system -

Laboratory tumor lysis syndrome: abnormality in two or more of the following, occurring within three days before or seven days after chemotherapy.

- uric acid > 475 μmol/l or 25% increase
- potassium > 6 mmol/l or 25% increase
- phosphate > 1.125 mmol/l or 25% increase
- calcium < 1.75 mmol/l or 25% decrease

Clinical tumor lysis syndrome: laboratory tumour lysis syndrome plus one or more of the following:

- increased serum creatinine (1.5 times upper limit of normal)
- cardiac arrhythmia or sudden death

- seizure

Next question >


B


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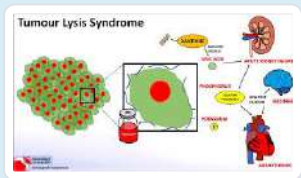


Textbooks



High-yield textbook


Extended textbook

Media






Tumour Lysis Syndrome

Oncology for Medical Students - YouTube  2  0



Tumour Lysis Syndrome in 3 Minutes

Townsend Teaching - YouTube  1  0



Tumour lysis syndrom

Score: **13.9%**

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A 50 year old woman was referred to haematology clinic for management of a persistent erythrocytosis that had been monitored by her General Practitioner over the previous 6 months. The patient was asymptomatic and in particular reported no headaches or visual changes. Past medical history was remarkable only for internal fixation of a tibial fracture sustained in a car accident 5 years previously. There is no strong family history of venous thrombosis or ischaemic heart disease. The patient took no regular medications and worked as an accountant. She is a life-long non-smoker and drinks approximately 10 units of alcohol per week.

Following assessment at haematology, further investigations were requested as listed below.

Hb	# g/dl
Platelets	# * 10 ⁹ /l
WBC	# * 10 ⁹ /l

Haemoglobin	18.7 g / dL
White cell count	6.1 * 10 ⁹ /l
Neutrophils	3.5 * 10 ⁹ /l
Lymphocytes	1.0 * 10 ⁹ /l
Monocytes	0.7 * 10 ⁹ /l
Eosinophils	0.4 * 10 ⁹ /l
Basophils	0.5 * 10 ⁹ /l
Platelets	276 * 10 ⁹ /l
Packed cell volume	0.57
Urea	4.5 mmol / L
Creatinine	95 micromol / L
Sodium	142 mmol / L
Potassium	4.5 mmol / L
Ferritin	56 ng / mL
Albumin	35 g / L
Alkaline phosphatase	80 U / L
ALT	20 U / L
Bilirubin	18 micromol / L
JAK 2 V617F mutation	Positive
Serum erythropoietin	3 U / L (reference 0-19)

Blood film: no abnormality detected

Abdominal ultrasound: liver, hepatic duct system and gallbladder unremarkable; mild-moderate splenomegaly; kidneys and renal tract unremarkable

What is the appropriate management for the patient's erythrocytosis?

- ☐ Aspirin and venesection with target PCV < 0.45 ×
- ☐ Aspirin and venesection with target PCV 0.45-0.50 ×
- ☐ Aspirin ×
- ☐ Venesection with target PCV 0.45-0.50 ×
- ☐ Hydroxyurea ×

Submit answer

Reference ranges ✓

Score: **12%**

- 1 ×
- 2 ×
- 3 ×
- 4 ×
- 5 ✓
- 6 ×
- 7 ×
- 8 ✓
- 9 ×
- 10 ×
- 11 ✓
- 12 ×
- 13 ×

14	×
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What is the appropriate management for the patient's erythrocytosis?

Aspirin and venesection with target PCV < 0.45	34%
Aspirin and venesection with target PCV 0.45-0.50	33%
Aspirin	4%
Venesection with target PCV 0.45-0.50	18%
Hydroxyurea	11%

This patient has polycythemia vera as evidenced by the positive JAK 2 mutation, normal blood film, splenomegaly and low serum erythropoietin.

Management of polycythemia depends on the patient's risk of thrombosis. This patient has a low risk of thrombosis based on her age, absence of cardiac risk factors, normal white cell and platelet count and absence of hyperviscosity symptoms.

The mainstay of treatment of polycythaemia vera is aspirin and venesection. A target PCV < 0.45 has been shown to have a significantly lower rate of death from cardiovascular disease and major thrombosis than target PCV 0.45-0.50. Treatment with aspirin reduces the risk of non-fatal myocardial infarction, non-fatal stroke, pulmonary embolus, major venous thrombosis or death from cardiovascular cause compared to placebo. Aspirin does not increase the incidence of major bleeding episodes compared to placebo.

Cytoreductive treatments such as hydroxyurea are used to treat high-risk polycythaemia vera.

Keohane C, McMullin M, Harrison C. The diagnosis and management of erythrocytosis. BMJ 2013;347:f6667.

   Discuss (5)  Improve

Next question >

Polycythaemia vera is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has a peak incidence in the sixth decade, with typical features including hyperviscosity, pruritus and splenomegaly.

Management

- aspirin
 - reduces the risk of thrombotic events
- venesection
 - first-line treatment to keep the haemoglobin in the normal range
- chemotherapy
 - hydroxyurea - slight increased risk of secondary leukaemia
 - phosphorus-32 therapy

Prognosis

- thrombotic events are a significant cause of morbidity and mortality
- 5-15% of patients progress to myelofibrosis
- 5-15% of patients progress to acute leukaemia (risk increased with chemotherapy treatment)



123



Next question >

B

I



A



T



Textbooks

High-yield textbook

Extended textbook

Links

Clinical Knowledge Summaries

[Polycythaemia guidelines](#)



9





4

[2005 polycythaemia guidelines](#)[Suggest link](#)[Report broken link](#)



Media

[What is polycythemia vera?](#)



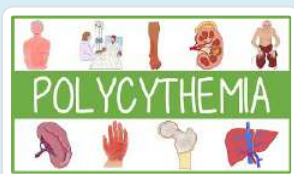
Khan Academy - YouTube

 4  0[Polycythemia vera](#)



Osmosis - YouTube

 1  0[Polycythemia Vera](#)

Medicosis Perfectionalis - YouTube

 0  0[Polycythemia: Clinical Features, Management and Mnemonics](#)

Townsend Teaching - YouTube

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94	✓
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Question 67 of 191



A 65-year-old male presents with a 2 year history of fatigue. Over the past year he has had progressive early satiety, vomiting and weight loss. On examination you note 10cm splenomegaly.

Investigation results are as follows:

Hb	84g/l	Na ⁺	138 mmol/l	Bilirubin	22 µmol/l
Platelets	65 * 10 ⁹ /l	K ⁺	3.7 mmol/l	ALP	88 u/l
WBC	2.2 * 10 ⁹ /l	Urea	4.5 mmol/l	ALT	22 u/l
Neuts	0.8 * 10 ⁹ /l	Creatinine	68 µmol/l	γGT	96 u/l
Lymphs	0.4 * 10 ⁹ /l			Albumin	28 g/l

Blood film: Tear-drop poikilocytes

What is the most likely diagnosis?

- ☐ Myelodysplasia due to bone marrow metastases ×
- ☐ Chronic myeloid leukaemia ×
- ☐ Acute myeloid leukaemia ×
- ☐ Myelofibrosis ×
- ☐ Megaloblastic anaemia ×

Submit answer

Reference ranges 

Score: **12%**

1 ×

2 ×

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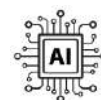
Blood film: Tear-drop poikilocytes

What is the most likely diagnosis?

Myelodysplasia due to bone marrow metastases	6%
Chronic myeloid leukaemia	4%
Acute myeloid leukaemia	2%
Myelofibrosis	87%
Megaloblastic anaemia	1%

Massive splenomegaly may early satiety and vomiting which can mimic gastric cancer

Important for me Less important



The blood results confirm pancytopenia with tear drop cells, suggestive of a primary marrow problem. Teardrop cells may be seen in the setting of marrow infiltration (by fibrosis, granulomatous inflammation, haematological or metastatic malignancy), splenic abnormalities, megaloblastic anaemia, and thalassemia.

In this case, the differential is clearly between gastric cancer (with bone marrow metastases resulting in myelodysplasia), and myelofibrosis. Early satiety and vomiting can be a feature of both

gastric cancer, and massive splenomegaly. The presence of splenomegaly, and the duration of symptoms are more suggestive of myelofibrosis.



Discuss (3)

Improve

Next question >

Myelofibrosis ★

Overview

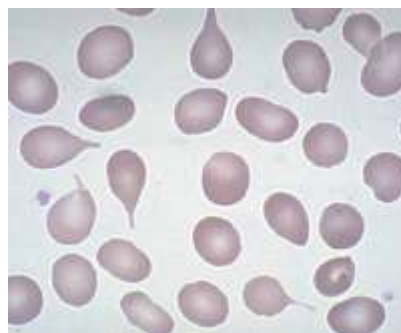
- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

Features

- e.g. elderly person with symptoms of anaemia e.g. fatigue (the most common presenting symptom)
- massive splenomegaly
- hypermetabolic symptoms: weight loss, night sweats etc

Laboratory findings

- anaemia
- high WBC and platelet count early in the disease
- 'tear-drop' poikilocytes on blood film
- unobtainable bone marrow biopsy - 'dry tap' therefore trephine biopsy needed
- high urate and LDH (reflect increased cell turnover)



Blood film showing the typical 'tear-drop' poikilocytes of myelofibrosis



123



B *I* **A** ▼ ▼ **T**↑ ▼ ▼

Textbooks

High-yield textbook

Extended textbook

Links

British Journal of Haematology

0 1

[Use of JAK inhibitors in the management of myelofibrosis](#)

[Suggest link](#)

[Report broken link](#)

Media



[Myelofibrosis](#)

Osmosis - YouTube

7 0



[Myelofibrosis](#)

Medicosis Perfectionalis - YouTube

3 1





Score: **13.9%**

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| 11 | ✓ |
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101	✗
102	-



A 56-year-old man presents to the clinic with a 1-week history of yellowing of his skin. He also complains of itching. A systematic inquiry was otherwise unremarkable. He drinks approximately 160 units of alcohol per week. Observations are within normal limits. On examination, there is palpable hepatosplenomegaly.

Blood results are as follows:

Hb	115 g/L	Male: (135-180) Female: (115 - 160)
Platelets	52 * 10 ⁹ /L	(150 - 400)
WBC	4.8 * 10 ⁹ /L	(4.0 - 11.0)
Reticulocytes	195 * 10 ⁹ /L	(50 - 100)
Urea	2.8 mmol/L	(2.0 - 7.0)
Creatinine	42 µmol/L	(55 - 120)
LDH	520 units/L	(140 - 280)
Haptoglobins	<0.5 g/L	(0.5 - 2.2)
Triglycerides	4.2 mmol/L	(<2.3)

Prothrombin time (PT)	16 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	38 secs	(25-35 secs)
Fibrinogen	2.8 g/L	(2 - 4)
D-Dimer	360 ng/mL	(< 400)

Bilirubin	58 µmol/L	(3 - 17)
ALP	580 u/L	(30 - 100)
ALT	126 u/L	(3 - 40)
Î³GT	860 u/L	(8 - 60)
Albumin	28 g/L	(35 - 50)

Direct antiglobulin test (DAT)	Negative
--------------------------------	----------

What is the treatment of choice?



Abstinence from alcohol



<input type="radio"/>	Eculizumab	×
<input type="radio"/>	Intravenous immunoglobulin (IVIg)	×
<input type="radio"/>	Plasma exchange	×
<input type="radio"/>	Prednisolone	×

Submit answer

Reference ranges ▾

Score: **12%**

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| 1 | × |
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| 3 | × |
| 4 | × |
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| 10 | × |
| 11 | ✓ |
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ALT	126 u/L	(3 - 40)
Î ³ GT	860 u/L	(8 - 60)
Albumin	28 g/L	(35 - 50)

Direct antiglobulin test (DAT)	Negative
--------------------------------	----------

What is the treatment of choice?

Abstinence from alcohol

63%

Ecuzumab	5%
Intravenous immunoglobulin (IVIg)	4%
Plasma exchange	7%
Prednisolone	21%

Zieve syndrome usually resolves with abstinence from alcohol

Important for me Less important

The presence of anaemia with reticulocytosis is suggestive of bleeding or haemolysis. The suppressed haptoglobins, raised bilirubin, and raised LDH are highly suggestive of haemolytic anaemia. The causes of haemolytic anaemia are wide and include hereditary (e.g. membranopathies, enzymopathies, haemoglobinopathies), immunological (e.g. autoimmune haemolytic anaemia), infective (e.g. malaria), and microangiopathic haemolytic anaemias (e.g. TTP, DIC).

It is also important to note that the patient is thrombocytopenic. The cause of this most likely relates to cirrhosis with portal hypertension and splenomegaly, given the significant alcohol history and the presence of hepatosplenomegaly. However, it may also be due to a recent alcohol binge since ethanol is toxic to platelets and can cause transient thrombocytopenia which should resolve within a few days following the binge. However, in the context of haemolytic anaemia, it would also be important to consider microangiopathic haemolytic anaemias (e.g. TTP, HUS, HELLP) which can cause thrombocytopenia due to platelet consumption.

The patient is also coagulopathic which is most certainly related to cirrhosis with decreased production of liver-derived clotting factors.

Abstinence from alcohol is correct. The most likely diagnosis is Zieve's syndrome (ZS) which is characterised by a triad of cholestatic jaundice (high ALP/GGT/bilirubin), DAT-negative haemolytic anaemia, and hyperlipidaemia that develops secondary to alcohol-induced liver injury (most commonly following a binge). The patient fulfils all the criteria of this triad favouring this diagnosis. The treatment for Zieve's syndrome is abstinence from alcohol. Abstinence from alcohol would also be essential for preventing the progression of cirrhosis.



Ecuzumab is incorrect. Ecuzumab is a terminal complement inhibitor that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. This drug is used to treat paroxysmal nocturnal haemoglobinuria (PNH). PNH presents with pancytopenia, intravascular haemolytic anaemia, and arterial/venous emboli. Although it remains within the differential diagnosis, the clinical and laboratory features are more in keeping with Zieve's syndrome.

Intravenous immunoglobulin (IVIg) is incorrect. IVIg can be used to treat autoimmune

haemolytic anaemia (AIHA). The patient clearly has haemolysis, however, the negative DAT makes AIHA an exceptionally unlikely diagnosis. Although DAT-negative haemolysis can occur it is exceedingly rare.

Plasma exchange is incorrect. Plasma exchange can be used to treat thrombotic thrombocytopenic purpura (TTP). Thrombotic thrombocytopenic purpura (TTP) is a microangiopathic haemolytic anaemia classically characterised by the pentad of fever, haemolytic anaemia, thrombocytopenia, and renal and neurologic dysfunction. Although it remains within the differential diagnosis, the clinical and laboratory features are more in keeping with Zieve's syndrome.

Prednisolone is incorrect. Prednisolone can be used to treat autoimmune haemolytic anaemia (AIHA). The patient clearly has haemolysis, however, the negative DAT makes AIHA an exceptionally unlikely diagnosis. Steroids can also be used to treat alcoholic hepatitis, however, the liver function tests are predominantly cholestatic in this case.

		 Discuss (3)	Improve
---	---	---	---------

Next question >

Haemolytic anaemias: by cause ★

Hereditary haemolytic anaemias can be subdivided into membrane, metabolism or haemoglobin defects

Hereditary causes

- membrane: hereditary spherocytosis/elliptocytosis
- metabolism: G6PD deficiency
- haemoglobinopathies: sickle cell, thalassaemia

Acquired haemolytic anaemias can be subdivided into immune and non-immune causes

Acquired: immune causes (Coombs-positive)

- autoimmune: warm/cold antibody type
- alloimmune: transfusion reaction, haemolytic disease newborn
- drug: methyldopa, penicillin

Acquired: non-immune causes (Coombs-negative)

- microangiopathic haemolytic anaemia (MAHA): TTP/HUS, DIC, malignancy, pre-eclampsia
- prosthetic heart valves
- paroxysmal nocturnal haemoglobinuria

- infections: malaria
- drug: dapsons
- Zieve syndrome
 - rare clinical syndrome of Coombs-negative haemolysis, cholestatic jaundice, and transient hyperlipidaemia associated with heavy alcohol use, typically following a binge
 - typically resolves with abstinence from alcohol



123



Next question >

B

I



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T

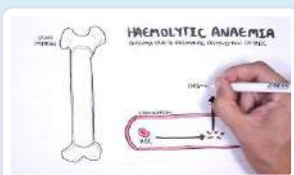


Textbooks

High-yield textbook

Extended textbook

Media



Haemolytic Anaemia - classification (intravascular, extravascular), pathophysiology, investigations

Armando Hasudungan - YouTube



3



2

Report broken media

Score: **13.9%**

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91	×
92	×
93	×
94	✓
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102	-



A 44-year-old woman presents to the clinic with bruising. This has progressively worsened over the past week. She has also been having frequent nose bleeds which self-terminate. Her past medical history includes rheumatoid arthritis for which she takes weekly methotrexate. She drinks approximately 64 units of alcohol per week.

Her observations are within normal limits. She is noted to have widespread petechia and purpura. On abdominal examination, there is palpable hepatosplenomegaly.

Blood results are as follows:

Hb	120 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$2 \times 10^9/L$	(150 - 400)
WBC	$8.0 \times 10^9/L$	(4.0 - 11.0)
Neuts	$6.0 \times 10^9/L$	(2.0 - 7.0)
Urea	5.4 mmol/L	(2.0 - 7.0)
Creatinine	75 $\mu\text{mol/L}$	(55 - 120)

Bilirubin	16 $\mu\text{mol/L}$	(3 - 17)
ALP	88 u/L	(30 - 100)
ALT	146 u/L	(3 - 40)
$\hat{\text{I}}^3\text{GT}$	582 u/L	(8 - 60)
Albumin	32 g/L	(35 - 50)

Prothrombin time (PT)	10 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	28 secs	(25-35 secs)
Fibrinogen	3.4 g/L	(2 - 4)
D-Dimer	360 ng/mL	(< 400)

What is the most likely cause of this patient's thrombocytopenia?

- ☐ Disseminated intravascular coagulation (DIC) ×
- ☐ Felty's syndrome ×
- ☐ Immune thrombocytopenic purpura (ITP) ×

☐ Portal hypertension ×

☐ Thrombotic thrombocytopenic purpura (TTP) ×

Submit answer

Reference ranges ▾

Score: **12%**

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Prothrombin time (PT)	10 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	28 secs	(25-35 secs)
Fibrinogen	3.4 g/L	(2 - 4)
D-Dimer	360 ng/mL	(< 400)

What is the most likely cause of this patient's thrombocytopenia?

Disseminated intravascular coagulation (DIC)	1%
Felty's syndrome	39%
Immune thrombocytopenic purpura (ITP)	48%

ITP should be considered in the presence of symptoms that suggest isolated thrombocytopenia e.g. epistaxis, menorrhagia

Important for me [Less important](#)

The causes of thrombocytopenia are wide and include decreased production (e.g. bone marrow failure), increased consumption (e.g. MAHA), and sequestration (e.g. portal hypertension with splenomegaly).

Immune thrombocytopenic purpura (ITP) is correct. ITP is an acquired autoimmune disorder characterised by a low platelet count resulting from peripheral platelet destruction by auto-antibodies. It can often be precipitated by malignancy, drugs, vaccinations, or infections. It is often commonly associated with other autoimmune disorders. A single-figure platelet count, with otherwise normal full blood count and a normal coagulation screen, is most likely a consequence of ITP.

Felty's syndrome is incorrect. Felty's syndrome is a rare, extra-articular manifestation of rheumatoid arthritis (RA), characterised by persistent, idiopathic neutropenia and, in some cases, splenomegaly. The absence of neutropenia makes this an unlikely diagnosis.

Disseminated intravascular coagulation (DIC) is incorrect. The normal coagulation profile excludes this diagnosis. DIC presents with prolonged PT, prolonged APTT, low fibrinogen and very high D-dimers.

Thrombotic thrombocytopenic purpura (TTP) is incorrect. Thrombotic thrombocytopenic purpura (TTP) is a microangiopathic haemolytic anaemia classically characterised by the pentad of fever, haemolytic anaemia, thrombocytopenia, and renal and neurologic dysfunction. The absence of any of the other criteria makes this an unlikely diagnosis.

Portal hypertension is incorrect. The patient certainly has features to suggest portal hypertension namely the significant alcohol history, deranged LFTs, and the presence of hepatosplenomegaly. Thrombocytopenia is a common complication in liver disease as a result of multiple factors, including splenic sequestration, reduced activity of the haematopoietic growth factor thrombopoietin, and bone marrow suppression by chronic hepatitis C virus infection. However, it is important to remember that the platelet count is rarely $< 50 \times 10^9/L$ in this setting. Therefore, although this may be a contributing factor in this clinical case, an alternative diagnosis should be considered, and indeed ITP is the most likely diagnosis.



Discuss (5)

Improve

Immune thrombocytopenia (ITP) in adults ★

Immune (or idiopathic) thrombocytopenic purpura (ITP) is an immune-mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb/IIIa or Ib-V-IX complex.

Children with ITP usually have an acute thrombocytopenia that may follow infection or vaccination. In contrast, adults tend to have a more chronic condition.

ITP in adults

Epidemiology

- more common in older females

Presentation

- may be detected incidentally following routine bloods
- symptomatic patients may present with
 - petechiae, purpura
 - bleeding (e.g. epistaxis)
 - catastrophic bleeding (e.g. intracranial) is not a common presentation

Investigations

- full blood count: isolated thrombocytopenia
- blood film
- a bone marrow examination is no longer used routinely
- antiplatelet antibody testing has poor sensitivity and doesn't affect clinical management so is not commonly done

Management

- first-line treatment for ITP is oral prednisolone
- pooled normal human immunoglobulin (IVIG) may also be used
 - it raises the platelet count quicker than steroids, therefore may be used if active bleeding or an urgent invasive procedure is required
- splenectomy is now less commonly used

Evan's syndrome

- ITP in association with autoimmune haemolytic anaemia (AIHA)

B *I* **A** ▼ ▼ **T**↑ ▼ ▼

Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

14 7

[2003 ITP guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Bleeding Disorders \(ITP vs TTP vs HUS vs DIC\)](#)

Dirty USMLE - YouTube

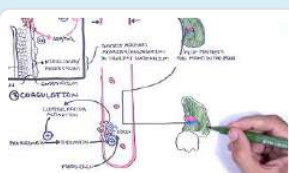
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[Immune thrombocytopenia \(ITP\)](#)

Osmosis - YouTube

4 0





[Report broken media](#)

Score: **13.9%**

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An 82-year-old man attends the clinic with a 6-month history of drenching night sweats and 10kg weight loss. He also complains of headaches and blurred vision. His observations are within normal limits. On examination, he has bulky bilateral cervical and inguinal lymphadenopathy.

Blood results are as follows:

Hb	115 g/L	Male: (135-180) Female: (115 - 160)
Platelets	185 * 10 ⁹ /L	(150 - 400)
WBC	7.2 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	135 mmol/L	(135 - 145)
K ⁺	4.4 mmol/L	(3.5 - 5.0)
Urea	6.2 mmol/L	(2.0 - 7.0)
Creatinine	85 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Total protein	110 g/L	(60-80)

What is the most likely diagnosis?

- ☐ Burkitt's lymphoma ×
- ☐ Diffuse large B-cell lymphoma ×
- ☐ Mantle cell lymphoma ×
- ☐ Marginal zone lymphoma ×
- ☐ Waldenstrom's macroglobulinaemia ×

Submit answer

Reference ranges 

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| 1 | ✗ |
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K ⁺	4.4 mmol/L	(3.5 - 5.0)
Urea	6.2 mmol/L	(2.0 - 7.0)
Creatinine	85 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Total protein	110 g/L	(60-80)

What is the most likely diagnosis?

Burkitt's lymphoma	8%
Diffuse large B-cell lymphoma	19%
Mantle cell lymphoma	4%
Marginal zone lymphoma	2%
Waldenstrom's macroglobulinaemia	67%

Weight loss, raised total protein, hyperviscosity symptoms (headache, blurring) → ?
Waldenstrom's macroglobulinaemia

Important for me Less important

Waldenstrom's macroglobulinaemia is correct. The clinical features are suggestive of lymphoma (e.g. B symptoms and lymphadenopathy). The presence of headaches, and visual impairment, in the context of a raised total protein, is suggestive of hyperviscosity. Although formal serum electrophoresis and immunofixation are required to confirm and classify the paraprotein, it is

usually IgM paraproteins that are implicated in hyperviscosity. This is because the IgM molecule is a massive pentameric structure. IgM paraproteins can be associated with many types of lymphoma, however, the classic cause is Waldenstrom's macroglobulinaemia, making this the most likely diagnosis.

Burkitt's lymphoma is incorrect. Burkitt's lymphoma is a highly aggressive high-grade lymphoma. It is the fastest-growing tumour seen in humans with a doubling time of between 24 and 48 hours. Thus the chronicity of the patient's symptoms makes this an exceptionally unlikely diagnosis.

Diffuse large B-cell lymphoma is incorrect. Diffuse large B cell lymphoma (DLBCL) is a highly aggressive high-grade lymphoma. Although not as rapidly growing as Burkitt's, the chronicity of the patient's symptoms makes this a less likely diagnosis.

Mantle cell lymphoma is incorrect. Although mantle cell lymphoma looks like a low-grade lymphoma under the microscope, it often behaves more like a high-grade lymphoma (e.g. rapid growth). Although it can occasionally produce an IgM paraprotein, it is Waldenstrom's macroglobulinaemia which is more commonly associated with IgM paraproteins making this the more likely diagnosis.

Marginal zone lymphoma is incorrect. There are three types of marginal zone lymphomas (MZL): extranodal MZL of mucosa-associated lymphoid tissue (MALT or gastric GALT), splenic MZL, and nodal MZL. Although IgM paraproteins are occasionally associated with MZL, they are much closer associated with Waldenstrom's macroglobulinaemia making this the favoured diagnosis.

		 Discuss (2)	Improve
---	---	---	---------

Next question >

Waldenstrom's macroglobulinaemia ★

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
 - the pentameric configuration of IgM increases serum viscosity
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Investigations

- monoclonal IgM paraproteinaemia

- bone marrow biopsy is diagnostic
 - infiltration of the bone marrow with lymphoplasmacytoid lymphoma cells

Management

- typically rituximab-based combination chemotherapy



+

Q

123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Media



Waldenstrom's macroglobulinaemia

Medicosis Perfectionalis - YouTube



6



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Waldenstrom's macroglobulinaemia

Osmosis - YouTube



5



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What is Waldenstrom's macroglobulinaemia

Khan Academy Medicine - YouTube 0 0

[Report broken media](#)

Score: **13.9%**

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A 70-year-old man is investigated for dysphagia and chest pain. These symptoms have been getting progressively worse for the past 3 months and have not responded to a trial of a proton pump inhibitor. There is no history of weight loss or anorexia.

On examination you note a left-sided partial ptosis. The patient also complains of double vision when you are assessing eye movements. Sustained upward gaze exacerbates his ptosis.

A chest x-ray is requested:



© Image used on license from Radiopaedia



What is the most likely diagnosis?

☐ Lung cancer



<input type="radio"/>	Cardiac myxoma	×
<input type="radio"/>	Tuberculosis	×
<input type="radio"/>	Sarcoidosis	×
<input type="radio"/>	Thymoma	×

Submit answer

Reference ranges ▾

Score: 12%		
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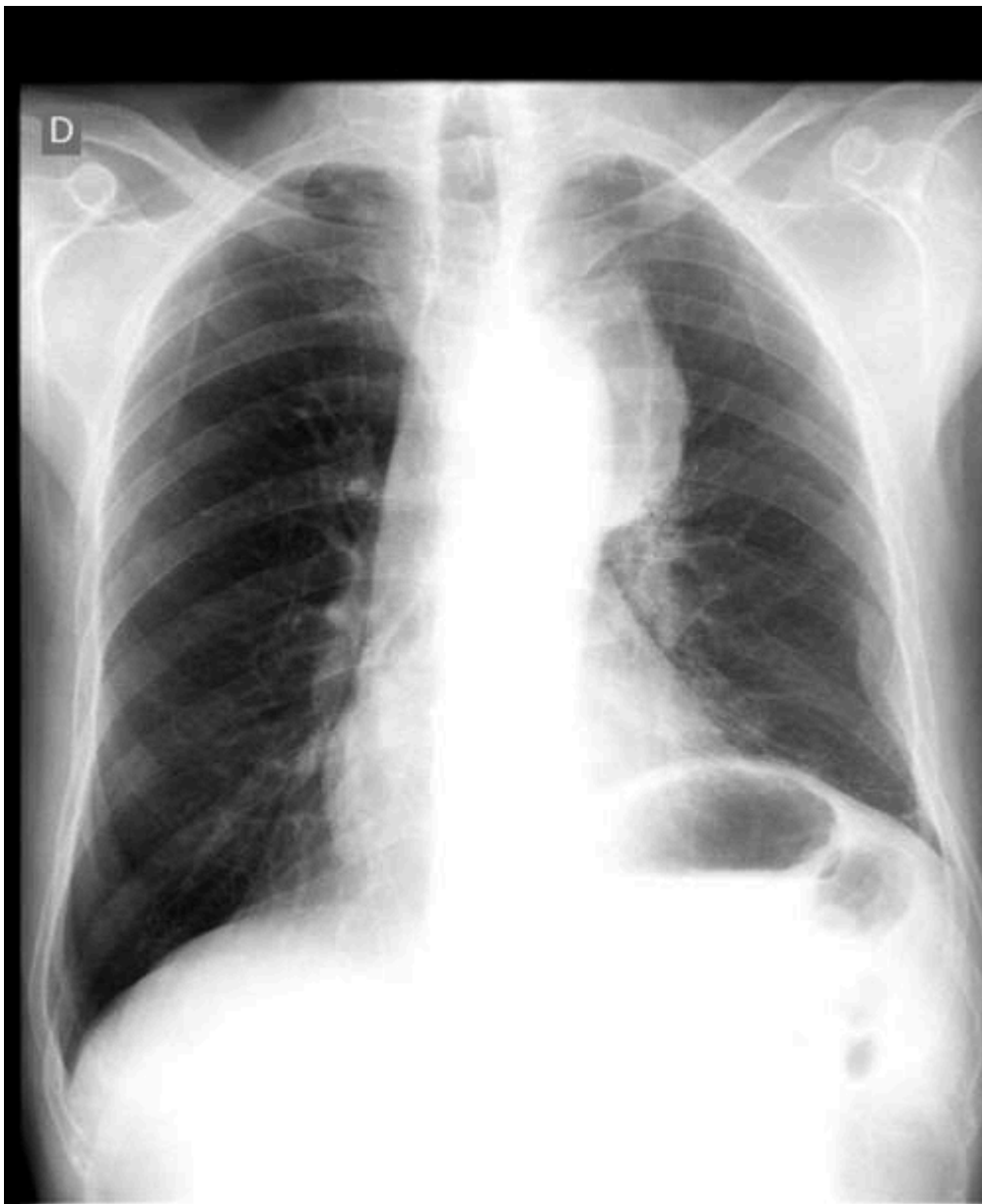
Question 71 of 191



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© Image used on license from Radiopaedia



What is the most likely diagnosis?

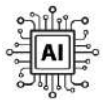
Lung cancer

11%

Cardiac myxoma	2%
Tuberculosis	0%
Sarcoidosis	1%
Thymoma	86%

Anterior mediastinal mass + symptoms of myasthenia = thymoma

Important for me [Less important](#)



The chest x-ray shows a partially delineated mediastinal mass (anterior mediastinum) with regular borders, bulging the left upper mediastinal contour. These findings are consistent with a thymoma.

The history is highly suggestive of myasthenia gravis which is seen in around a third of patients with a thymoma. Note how the ptosis worsened with sustained upward gaze, a demonstration of fatigability.

Discuss (5)

Improve

[Next question >](#)

Thymoma ★

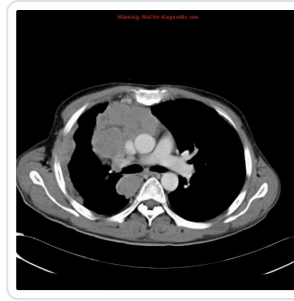
Thymomas are the most common tumour of the anterior mediastinum and is usually detected between the sixth and seventh decades of life.

Associated with

- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death

- compression of airway
- cardiac tamponade



123



Next question >

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Textbooks

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Links

Radiopaedia



8



3

[Thymic tumours](#)

[Suggest link](#)

[Report broken link](#)

Score: **13.9%**

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102	-



A 53-year-old man presents to the emergency department with a rash and ulceration on his lower limbs. He has a past medical history of untreated hepatitis C virus. He is not on any regular medications. He is homeless. He is an intravenous drug user.

On examination, there is a purpuric rash on his lower limbs with ulceration of the digits. There is no clinical evidence of synovitis.

Blood tests:

Hb	121 g/L	Male: (135-180) Female: (115 - 160)
Platelets	422 * 10 ⁹ /L	(150 - 400)
WBC	5.2 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	141 µmol/L	(55 - 120)
CRP	55 mg/L	(< 5)
Rheumatoid factor	654 IU/ml	(0-20)
Complement (C3)	0.81 g/L	(0.75 - 1.65)
Complement (C4)	.02 g/L	(0.16 to 0.48)
Antinuclear antibody	negative	(negative)
ESR	101 mm/Hr	(0-20)
IgA	10.2 g/L	(6.60 - 15.90)
IgG	24.1 g/L	(6-16)
IgM	4.2 g/L	(0.53-2.47)

Urinalysis:

Leucocytes	negative
Nitrites	negative
Blood	+++
Protein	++
Glucose	negative

What is the likely diagnosis?

<input type="radio"/>	Rheumatoid vasculitis	×
<input type="radio"/>	Systemic lupus erythematosus	×
<input type="radio"/>	Type I cryoglobulinaemia	×
<input type="radio"/>	Type II cryoglobulinaemia	×
<input type="radio"/>	Type III cryoglobulinaemia	×

Submit answer

Reference ranges ▾

Score: 12%

1	×
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Urinalysis:

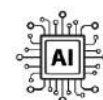
Leucocytes	negative
Nitrites	negative
Blood	+++
Protein	++
Glucose	negative

What is the likely diagnosis?

Rheumatoid vasculitis	1%
Systemic lupus erythematosus	1%
Type I cryoglobulinaemia	21%
Type II cryoglobulinaemia	71%
Type III cryoglobulinaemia	6%

Hepatitis C is associated with mixed (type II) cryoglobulinaemia

Important for me [Less important](#)



Type II cryoglobulinaemia is correct. This patient presents with a purpuric rash on the lower limbs with distal ulceration in association with hypocomplementaemia and a positive rheumatoid factor on a background of hepatitis C. This suggests a diagnosis of cryoglobulinaemia. Hepatitis C is associated with Type II cryoglobulinaemia. The haematoproteinuria and deranged renal function suggest glomerulonephritis. Rheumatoid factor may be very high in this condition.

Rheumatoid vasculitis is incorrect. This may cause a rash, ulceration and positive rheumatoid factor. However, it tends not to cause low complement and glomerulonephritis and is, therefore, less likely. Additionally, it tends to occur in longstanding rheumatoid, which is absent here.

Systemic lupus erythematosus is incorrect. This can be associated with rash, low complement, rheumatoid factor and ulceration. However, a negative ANA essentially excludes the diagnosis.

Type I cryoglobulinaemia is incorrect. This form of cryoglobulinaemia is typically associated with a monoclonal IgM or IgG rather than a polyclonal picture. It is associated with multiple myeloma and Waldenstrom's macroglobulinaemia.

Type III cryoglobulinaemia is incorrect. This type of cryoglobulinaemia is typically associated with rheumatoid arthritis and Sjogren's rather than hepatitis C. The absence of joint symptoms and the negative ANA make rheumatoid arthritis and Sjogren's unlikely.

Discuss (3) [Improve](#)

[Next question >](#)

Cryoglobulinaemia ★

Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C. One-third of cases are idiopathic

Three types

- type I (25%):
 - monoclonal - IgG or IgM
 - associations: multiple myeloma, Waldenstrom macroglobulinaemia
- type II (25%)
 - mixed monoclonal and polyclonal: usually with rheumatoid factor
 - associations: hepatitis C, rheumatoid arthritis, Sjogren's, lymphoma
- type III (50%)
 - polyclonal: usually with rheumatoid factor
 - associations: rheumatoid arthritis, Sjogren's

Possible features

- Raynaud's only seen in type I
- cutaneous
 - vascular purpura
 - distal ulceration
 - ulceration
- arthralgia
- renal involvement
 - diffuse glomerulonephritis

Investigations

- low complement (esp. C4)
- high ESR

Management

- treatment of underlying condition e.g. hepatitis C
- immunosuppression
- plasmapheresis



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Next question >

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Score: **13.9%**

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100	×
101	×
102	-



A 19-year-old African male was referred by his GP to the medical assessment unit with a complaint of dark coloured urine, abdominal pain and jaundice. He does not have any other co-morbidities and there is no family history of haemolytic anaemias. He recently tried a new Mediterranean diet containing fava beans. On examination, there is moderate splenomegaly.

Hb	70 g/l	Na ⁺	137 mmol/l	Bilirubin	107 µmol/l
Platelets	280 * 10 ⁹ /l	K ⁺	4.3 mmol/l	ALP	98 u/l
WBC	8.7* 10 ⁹ /l	Urea	5.6 mmol/l	ALT	25 u/l
Neuts	5.6 * 10 ⁹ /l	Creatinine	77 µmol/l	γGT	37 u/l
Lymphs	1.3 * 10 ⁹ /l			Albumin	35 g/l
Eosin	0.9 * 10 ⁹ /l				

Serum haptoglobin was undetectable, and serum lactate dehydrogenase (LDH) was 1987 units/l. Peripheral blood film showed Heinz bodies. A direct Coombe's test was negative. G6PD levels return as normal.

What investigation should be performed next to confirm the diagnosis?

- ☐ Repeat G6PD level immediately as the first specimen may have been inadequate ×
- ☐ Ultrasound abdomen ×
- ☐ Hepatitis serology ×
- ☐ Bone marrow examination ×
- ☐ G6PD analysis in few weeks when symptoms improved ×

Submit answer

Reference ranges 

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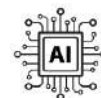
Serum haptoglobin was undetectable, and serum lactate dehydrogenase (LDH) was 1987 units/l. Peripheral blood film showed Heinz bodies. A direct Coombe's test was negative. G6PD levels return as normal.

What investigation should be performed next to confirm the diagnosis?

Repeat G6PD level immediately as the first specimen may have been inadequate	10%
Ultrasound abdomen	1%
Hepatitis serology	1%
Bone marrow examination	4%
G6PD analysis in few weeks when symptoms improved	84%

G6PD deficiency: G6PD level may be normal during an acute haemolytic episode

Important for me Less important



G6PD testing should be performed when patients are in remission as the result may be falsely negative during acute haemolysis. The reason for this is that during an acute haemolytic episode, older erythrocytes with low G6PD levels are destroyed and there is a compensatory increase in immature erythrocytes and reticulocytes that have increased G6PD levels.

Although ultrasound abdomen may be useful in assessing for splenomegaly and gallstones in this patient, it's not diagnostic of G6PD deficiency.

Hepatitis serology is more useful in the setting of jaundice secondary to hepatobiliary disease.

Bone marrow examination is not an investigation of choice in G6PD deficiency.

		 Discuss (4)	Improve
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Next question >

G6PD deficiency ★

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in an X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

Pathophysiology

- G6PD is the first step in the pentose phosphate pathway, which converts glucose-6-phosphate → 6-phosphogluconolactone
 - this reaction also results in nicotinamide adenine dinucleotide phosphate (NADP) → NADPH
 - i.e. $\text{glucose-6-phosphate} + \text{NADP} \rightarrow \text{6-phosphogluconolactone} + \text{NADPH}$
- NADPH is important for converting oxidized glutathione back to its reduced form
- reduced glutathione protects red blood cells from oxidative damage by oxidants such as superoxide anion (O_2^-) and hydrogen peroxide
- $\downarrow \text{G6PD} \rightarrow \downarrow \text{reduced NADPH} \rightarrow \downarrow \text{reduced glutathione} \rightarrow \text{increased red cell susceptibility to oxidative stress}$

Features

- neonatal jaundice is often seen
- intravascular haemolysis
- gallstones are common
- splenomegaly may be present
- Heinz bodies on blood films. Bite and blister cells may also be seen

Diagnosis is made by using a G6PD enzyme assay

- levels should be checked around 3 months after an acute episode of hemolysis, RBCs with the most severely reduced G6PD activity will have hemolysed → reduced G6PD activity → not be measured in the assay → false negative results

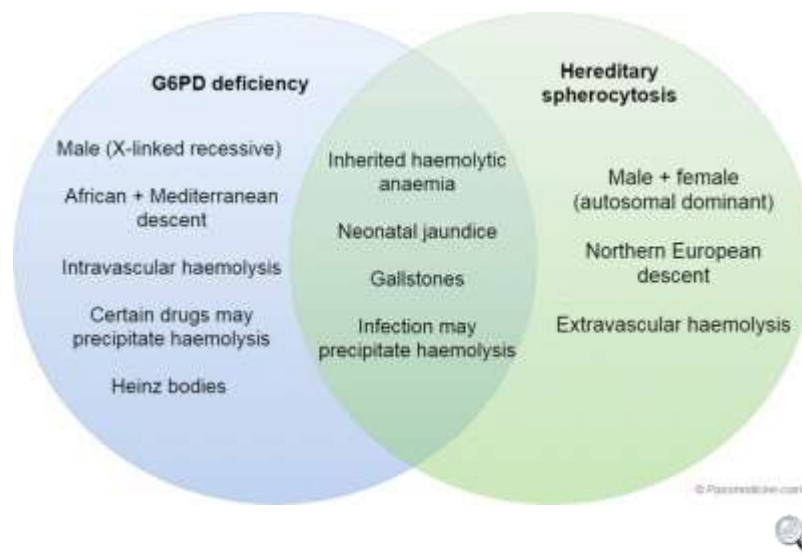
Some drugs causing haemolysis

- anti-malarials: primaquine
- ciprofloxacin
- sulph- group drugs: sulphonamides, sulphasalazine, sulfonylureas

Some drugs thought to be safe

- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

Comparing G6PD deficiency to hereditary spherocytosis:



Comparison of G6PD deficiency to hereditary spherocytosis

	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent
Typical history	<ul style="list-style-type: none">• Neonatal jaundice• Infection/drugs precipitate haemolysis• Gallstones	<ul style="list-style-type: none">• Neonatal jaundice• Chronic symptoms although haemolytic crises may be precipitated by infection• Gallstones• Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	EMA binding



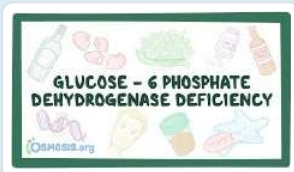
123

[Next question >](#)**B***I***A****T**

Textbooks

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Media

[Glucose-6-Phosphate Dehydrogenase \(G6PD\) deficiency](#)

Osmosis - YouTube

7 0

[Glucose-6-Phosphate Dehydrogenase \(G6PD\) deficiency](#)

Medicosis Perfectionalis - YouTube

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[Report broken media](#)Score: **13.9%**

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Question 74 of 191



A 72-year-old man is brought into the emergency department following a fall. He was found by his daughter unresponsive on the floor after hearing a loud bang. His daughter tells you that he has been more unsteady on his feet for the last few days and is recovering from a urinary tract infection. There is a past medical history of benign prostatic hyperplasia and atrial fibrillation for which he takes tamsulosin, finasteride and rivaroxaban.

On examination, he is drowsy with a GCS of 12 (E3V4M5). He has a heart rate of 85bpm and blood pressure of 210/118mmHg. On auscultation, his chest is clear with normal heart sounds. Oxygen saturations are 90% on air. There is a deep laceration over the left side of his forehead which is oozing blood and there is bruising down the left side of his body. Pupils are equal and reactive to light.

CT Head: Evidence of a moderate intracranial haemorrhage in the left frontal lobe. There is no evidence of a mass effect.


What is the most appropriate next step in the management of this patient?


- | | |
|---------------------------------------|---|
| <input type="radio"/> Andexanet alfa | × |
| <input type="radio"/> Cryoprecipitate | × |
| <input type="radio"/> Dexamethasone | × |
| <input type="radio"/> Idarucizumab | × |
| <input type="radio"/> Protamine | × |

Submit answer

Reference ranges 

Score: 12%

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8	✓
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CT Head: Evidence of a moderate intracranial haemorrhage in the left frontal lobe. There is no evidence of a mass effect.

What is the most appropriate next step in the management of this patient?

Andexanet alfa	70%
Cryoprecipitate	6%
Dexamethasone	3%
Idarucizumab	18%
Protamine	2%

Rivaroxaban and apixaban can be reversed by andexanet alfa

Important for me Less important

This patient has had a traumatic intracranial haemorrhage. Initial treatment should be to maintain a patent airway and attempt to stop the bleeding in order to prevent raised intracranial pressures. With patients taking anticoagulant therapy, actions should be taken to reverse their action. Andexanet alfa is a recombinant form of factor Xa which binds specifically to apixaban or rivaroxaban to reverse their anticoagulant effects.

Cryoprecipitate is derived from fresh frozen plasma and contains factor VIII, factor XIII, fibrinogen, vWF and fibronectin. It is used to treat fibrinogen deficiency in cases of disseminated intravascular coagulation, trauma, invasive procedures or haemorrhage. It is more commonly used to treat an

intracranial haemorrhage secondary to tissue plasminogen activator use for an acute ischaemic stroke.

Dexamethasone can be given in the case of increased intracranial pressure, which can be secondary to intracranial haemorrhage and subsequent mass effect. However, the current investigations do not show evidence of cerebral oedema or midline shift and therefore dexamethasone is not the next initial treatment to be given.

Idarucizumab is a specific reversal agent for dabigatran. As this patient is not taking dabigatran therapy, the use of idarucizumab is not indicated.

Protamine is used in the reversal of heparin. As this patient is not taking heparin therapy, the use of protamine is not indicated.

   Discuss (4) [Improve](#)

[Next question >](#)

Direct oral anticoagulants ★

Direct oral anticoagulants (DOACs) are currently used for the following indications:

- prevention of stroke in non-valvular AF. NICE stipulate that certain other risk factors should be present. These are complicated and differ between the DOACs but generally require one of the following to be present:
 - prior stroke or transient ischaemic attack
 - age 75 years or older
 - hypertension
 - diabetes mellitus
 - heart failure
- prevention of VTE following hip/knee surgery
- treatment of DVT and PE

The table below summaries some of the differences between the DOACs:

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Excretion	Majority renal	Majority liver	Majority faecal	Majority faecal

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Reversal	Idarucizumab	Andexanet alfa*	Andexanet alfa*	No authorised reversal agent, although andexanet alfa has been studied

*Andexanet alfa is a recombinant form of human factor Xa protein

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Next question >


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Royal College of Physicians

Drug therapy in anticoagulation: which drug for which patient?

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NICE

2012 Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation

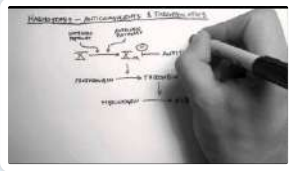
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Antiplatelets and anticoagulants made easy

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Score: **13.9%**

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96	×
97	×
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Question 75 of 191



A 24-year-old female presents to her GP with a 2 month history of tiredness. On further questioning she admits she has also been experiencing pain in the centre of her chest and in the lymph nodes in her neck when drinking alcohol.

What is the likely underlying cause?

- ☐ Hodgkin's lymphoma ×
- ☐ Somatisation disorder ×
- ☐ GORD (gastro-oesophageal reflux disease) ×
- ☐ Hiatus hernia ×
- ☐ Pancreatitis ×

Submit answer

Reference ranges 

Score: 12%

- 1 ×
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Question 75 of 191



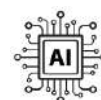
A 24-year-old female presents to her GP with a 2 month history of tiredness. On further questioning she admits she has also been experiencing pain in the centre of her chest and in the lymph nodes in her neck when drinking alcohol.

What is the likely underlying cause?

Hodgkin's lymphoma	88%
Somatisation disorder	6%
GORD (gastro-oesophageal reflux disease)	3%
Hiatus hernia	1%
Pancreatitis	1%




Lymph node pain when drinking alcohol is very specific for Hodgkin's lymphoma (although it occurs rarely)

Important for me [Less important](#)



Lymph node pain when drinking alcohol is very specific for Hodgkin's lymphoma. It is however a rare symptoms and most patients do not experience it.

None of the other conditions mentioned cause pain in lymph nodes



 Discuss (5)
 [Improve](#)

[Next question >](#)

Hodgkin's lymphoma: presentation ★

Hodgkin's lymphoma (HL) is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Risk factors

- HIV
- Epstein-Barr virus

Features

- lymphadenopathy (75%)
 - most commonly in the neck (cervical/supraclavicular) > axillary > inguinal
 - usually painless, non-tender, asymmetrical
 - alcohol-induced lymph node pain is characteristic of Hodgkin's lymphoma but is seen in less than 10% of patients
- systemic - 'B symptoms' (25%)
 - weight loss
 - pruritus
 - night sweats
 - fever (Pel-Ebstein)
- other possible presentations include a mediastinal mass
 - may be symptomatic (e.g. cough) or found incidentally on a chest x-ray

Investigations

- normocytic anaemia
 - may be multifactorial e.g. hypersplenism, bone marrow replacement by HL, Coombs-positive haemolytic anaemia etc
- eosinophilia
 - caused by the production of cytokines e.g. IL-5
- LDH raised
- lymph node biopsy
 - Reed-Sternberg cells are diagnostic: these are large cells that are either multinucleated or have a bilobed nucleus with prominent eosinophilic inclusion-like nucleoli (thus giving an 'owl's eye' appearance)



123



Next question >

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Clinical Knowledge Summaries

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[Hodgkin's lymphoma](#)

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[Hodgkin's lymphoma](#)

Osmosis - YouTube 👍 0 🗑️ 0



[Hodgkin's Lymphoma Mnemonic](#)

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Score: **13.9%**

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You are the medical registrar on call. The surgical registrar contacts you for a patient he has just seen in clinic who requires an elective cholecystectomy. The patient is a 65-year-old woman who has atrial fibrillation for which she takes rivaroxaban. The patient is otherwise well. The bloods performed in clinic that day are as follows:

Hb	131 g/l
Platelets	$352 \times 10^9/l$
WBC	$5.5 \times 10^9/l$
INR	1.5

Na ⁺	137 mmol/l
K ⁺	3.6 mmol/l
Urea	3.2 mmol/l
Creatinine	67 μ mol/l

The surgical registrar would like to know how long the patient should omit their anticoagulation before the procedure?

- ☐ 1 day ×
- ☐ 2 days ×
- ☐ 3 days ×
- ☐ 5 days ×
- ☐ 7 days ×

Submit answer

Reference ranges 

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K^+	3.6 mmol/l
Urea	3.2 mmol/l
Creatinine	67 μ mol/l

The surgical registrar would like to know how long the patient should omit their anticoagulation before the procedure?

1 day	31%
2 days	30%
3 days	15%
5 days	14%
7 days	9%

The new oral anticoagulant drugs (NOACs) are being used increasingly in patients who require anticoagulation. They have the advantage of once or twice daily dosing regimes, oral formulation and do not require therapeutic monitoring like warfarin. They are particularly useful in patients that may have issues with warfarin compliance or those with erratic international normalised ratio (INR) readings. NOACs have been shown to convey equivalent efficacy to warfarin in most contexts the main exception being anticoagulation in patients with prosthetic heart valves where NOACs were not as effective as warfarin.

Rivaroxaban is one of the most commonly used agents. It acts as a direct factor Xa inhibitor. It is

absorbed from the gut and has maximum factor Xa inhibition four hours post dose. It is indicated for anticoagulation in atrial fibrillation and in the treatment of venous thromboembolism. It has a half-life of 7-9 hours and is metabolised in the liver. Factor Xa levels do not return to normal for just over 24 hours so once daily dosing is appropriate.

The following table outlines how long anticoagulants need to be withheld before surgery:

Drug	Duration to withhold before procedure
Dabigatran	1-2 days with creatinine clearance >50ml/min
Rivaroxaban	1 day if creatinine clearance >90 ml/min
Apixaban	1-2 days if creatinine clearance >60
Fondaparinux	36-48 hours
LMWH	12 hrs for prophylactic dose, 24 hours for therapeutic dose
Warfarin	1-8 days, check INR
UFH	IV 4-6 hrs, SC 12-24 hrs



Discuss (10)

Improve

Next question >

Direct oral anticoagulants ★

Direct oral anticoagulants (DOACs) are currently used for the following indications:

- prevention of stroke in non-valvular AF. NICE stipulate that certain other risk factors should be present. These are complicated and differ between the DOACs but generally require one of the following to be present:
 - prior stroke or transient ischaemic attack
 - age 75 years or older
 - hypertension
 - diabetes mellitus
 - heart failure
- prevention of VTE following hip/knee surgery
- treatment of DVT and PE

The table below summaries some of the differences between the DOACs:

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Excretion	Majority renal	Majority liver	Majority faecal	Majority faecal
Reversal	Idarucizumab	Andexanet alfa*	Andexanet alfa*	No authorised reversal agent, although andexanet alfa has been studied

*Andexanet alfa is a recombinant form of human factor Xa protein



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[Drug therapy in anticoagulation: which drug for which patient?](#)

NICE

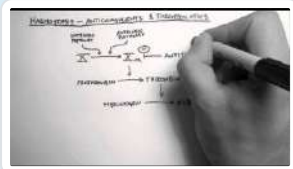
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Media





Haemostasis 3 - Anticoagulants & Thrombolytics

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







Antiplatelets and anticoagulants made easy

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Question 77 of 191



A 45-year-old worker on demolition sites comes to the Emergency department for review. He has suffered increasing tiredness, lethargy, headache, and abdominal pains over the past 2 months. On examination he is hypertensive with a blood pressure of 155/90 mmHg, his pulse is 85 beats per minute and regular. He looks pale.

Investigations

Hb	97 g/l
MCV	78 fl
Platelets	$175 \times 10^9/l$
WBC	$6.2 \times 10^9/l$
Lead	5 $\mu\text{mol/l}$

Blood film reveals basophilic stippling

Which of the following is the most appropriate initial intervention?

- ☐ Activated charcoal ×
- ☐ Disodium EDTA ×
- ☐ DMSA ×
- ☐ Haemodialysis ×
- ☐ Vitamin C ×

Submit answer

Reference ranges 

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| 4 | ✗ |
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Question 77 of 191



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Investigations

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MCV	78 fl
Platelets	$175 \times 10^9/l$
WBC	$6.2 \times 10^9/l$
Lead	5 $\mu\text{mol/l}$

Blood film reveals basophilic stippling

Which of the following is the most appropriate initial intervention?

Activated charcoal	2%
Disodium EDTA	34%
DMSA	55%
Haemodialysis	5%
Vitamin C	5%

DMSA is an oral chelation therapy that can be used for chronic lead poisoning, the diagnosis here. A lead level above 3.4 $\mu\text{mol/l}$ indicates significant occupational exposure and that the patient should be withdrawn from work. 500mg twice per day is a usual initial therapeutic dose.

Given his lead exposure represents chronic exposure, there is no role for activated charcoal. Disodium EDTA is used in the management of acute lead poisoning and is given intravenously. Human trials of vitamin C with respect to treatment of lead toxicity are so far equivocal, and there is no role for haemodialysis in chronic lead poisoning.

[Discuss \(1\)](#)[Improve](#)[Next question >](#)

Lead poisoning ★

Along with acute intermittent porphyria, lead poisoning should be considered in questions giving a combination of abdominal pain and neurological signs. Lead poisoning results in defective ferrochelatase and ALA dehydratase function.

Features

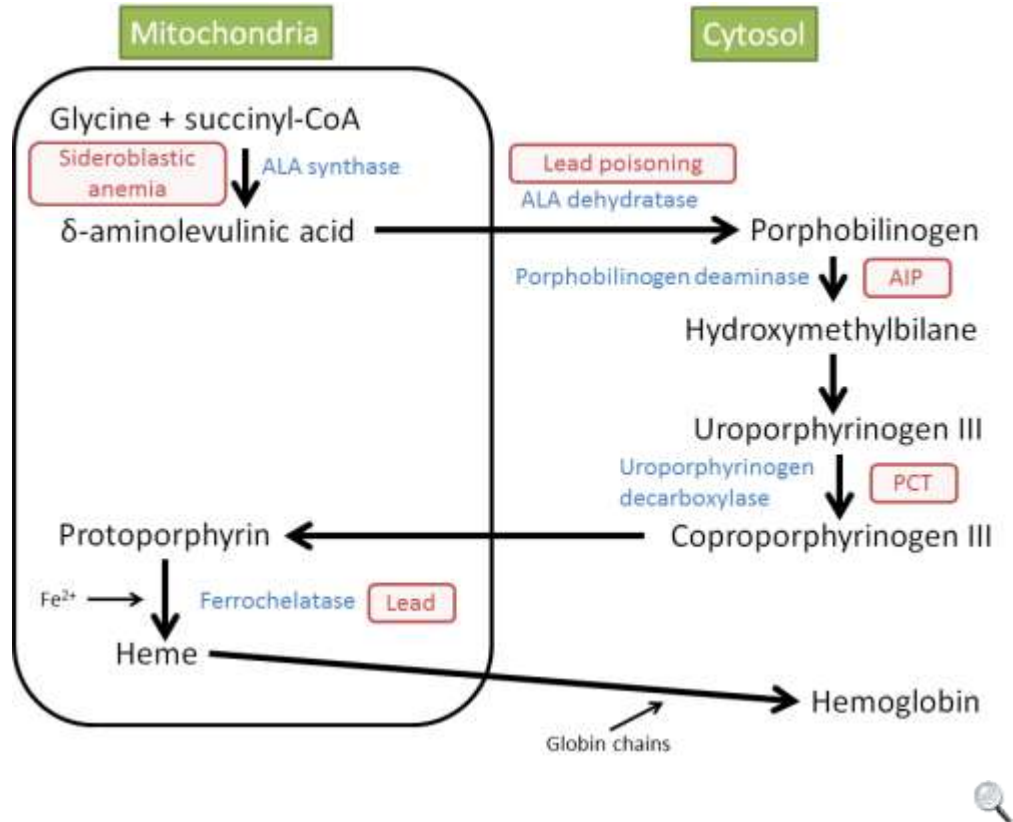
- abdominal pain
- peripheral neuropathy (mainly motor)
- neuropsychiatric features
- fatigue
- constipation
- blue lines on gum margin (only 20% of adult patients, very rare in children)

Investigations

- the blood lead level is usually used for diagnosis. Levels greater than 10 mcg/dl are considered significant
- full blood count: microcytic anaemia. Blood film shows red cell abnormalities including basophilic stippling and clover-leaf morphology
- raised serum and urine levels of delta aminolaevulinic acid may be seen making it sometimes difficult to differentiate from acute intermittent porphyria
- urinary coproporphyrin is also increased (urinary porphobilinogen and uroporphyrin levels are normal to slightly increased)
- in children, lead can accumulate in the metaphysis of the bones although x-rays are not part of the standard work-up

Management - various chelating agents are currently used:

- dimercaptosuccinic acid (DMSA)
- D-penicillamine
- EDTA
- dimercaprol



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123



Next question >

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Score: **13.9%**

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82	×
83	×
84	×
85	✓
86	×
87	×
88	×
89	×
90	×
91	×
92	×
93	×
94	✓
95	×
96	×
97	×
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99	×
100	×
101	×
102	-



A 65-year-old man is seen in the haematology clinic for review of test results. He has been fatigued for the last three months and has experienced night sweats. On examination he is pale with a palpable spleen 4cm below the costal margin, mildly tender on palpation. His only other past medical history is of osteoarthritis.

His results are as follows:

Hb	89 g/l	Na ⁺	140 mmol/l
Platelets	205 * 10 ⁹ /l	K ⁺	4.0 mmol/l
WBC	5 * 10 ⁹ /l	Urea	5.8 mmol/l
Neuts	3.6 * 10 ⁹ /l	Creatinine	72 µmol/l
Lymphs	1.2 * 10 ⁹ /l	CRP	3 mg/l

Blood film: Anisocytosis with mild hypochromia. Tear drop cells.

CT chest/abdomen/pelvis: Splenic enlargement. No suspicious mass lesions seen. 1cm simple right renal cyst. No lymphadenopathy.

Bone marrow biopsy: Fibrosis

Which initial therapy should be used to treat this gentleman?

- ☐ Chlorambucil ×
- ☐ Fludarabine ×
- ☐ Hydroxycarbamide ×
- ☐ Interferon alpha ×
- ☐ Lenalidomide ×

Submit answer

Reference ranges ∨

- | | |
|----|---|
| 1 | ✗ |
| 2 | ✗ |
| 3 | ✗ |
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| 8 | ✓ |
| 9 | ✗ |
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| 11 | ✓ |
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Question 78 of 191



A 65-year-old man is seen in the haematology clinic for review of test results. He has been fatigued for the last three months and has experienced night sweats. On examination he is pale with a palpable spleen 4cm below the costal margin, mildly tender on palpation. His only other past medical history is of osteoarthritis.

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Blood film: Anisocytosis with mild hypochromia. Tear drop cells.

CT chest/abdomen/pelvis: Splenic enlargement. No suspicious mass lesions seen. 1cm simple right renal cyst. No lymphadenopathy.

Bone marrow biopsy: Fibrosis

Which initial therapy should be used to treat this gentleman?

Chlorambucil	13%
Fludarabine	16%
Hydroxycarbamide	47%
Interferon alpha	11%
Lenalidomide	13%

This gentleman has myelofibrosis as evidenced by bone marrow fibrosis, tear drop cells on blood film and constitutional symptoms. He has symptomatic splenomegaly and anaemia. First line treatment for this would be hydroxycarbamide.

Chlorambucil is used in chronic lymphocytic leukaemia and non-Hodgkin lymphoma. Fludarabine is used to treat acute myeloid leukaemia. Interferon alpha is used for myelosuppression in

myelofibrosis in the presence of thrombocytosis or leucocytosis. Lenalidomide is used in the treatment of multiple myeloma.

Use of JAK inhibitors in the management of myelofibrosis: a revision of the British Committee for Standards in Haematology Guidelines for Investigation and Management of Myelofibrosis 2012. British Journal of Haematology, 2014;:167;418438.



Discuss (9)

Improve

Next question >

Myelofibrosis ★

Overview

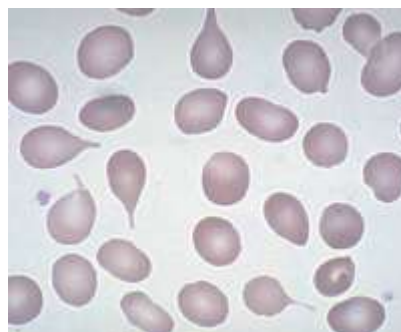
- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

Features

- e.g. elderly person with symptoms of anaemia e.g. fatigue (the most common presenting symptom)
- massive splenomegaly
- hypermetabolic symptoms: weight loss, night sweats etc

Laboratory findings

- anaemia
- high WBC and platelet count early in the disease
- 'tear-drop' poikilocytes on blood film
- unobtainable bone marrow biopsy - 'dry tap' therefore trephine biopsy needed
- high urate and LDH (reflect increased cell turnover)



Blood film showing the typical 'tear-drop' poikilocytes of myelofibrosis



123

[Next question >](#)**B***I***A****T**

Textbooks

[High-yield textbook](#)[Extended textbook](#)

Links

[British Journal of Haematology](#)

0



1

[Use of JAK inhibitors in the management of myelofibrosis](#)[Suggest link](#)[Report broken link](#)

Media

[Myelofibrosis](#)

Osmosis - YouTube



7



0

[Myelofibrosis](#)

Medicosis Perfectionalis - YouTube



3



1



Myelofibrosis

Armando Hasudungan - YouTube

 5  2

[Report broken media](#)

Score: **13.9%**

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| 1 | ✗ |
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Question 79 of 191



A 30-year-old lady presents with shortness of breath and facial flushing. She had been to a restaurant that evening and noticed the symptoms when rushing home. She also had itchy skin and tingling lips. On examination she was tachycardic with a wheeze. She had no history of food allergies and reported eating lasagne for dinner alongside a glass of wine. What is the most likely diagnosis?

- | | | |
|-----------------------|-----------------------------------|---|
| <input type="radio"/> | Acute asthma attack | × |
| <input type="radio"/> | Carcinoid syndrome | × |
| <input type="radio"/> | Exercise induced wheat angioedema | × |
| <input type="radio"/> | Shellfish anaphylaxis | × |
| <input type="radio"/> | Thyrotoxicosis | × |

Submit answer

Reference ranges ▾

Score: **12%**

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| 1 | × |
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| 10 | × |
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A 30-year-old lady presents with shortness of breath and facial flushing. She had been to a restaurant that evening and noticed the symptoms when rushing home. She also had itchy skin and tingling lips. On examination she was tachycardic with a wheeze. She had no history of food allergies and reported eating lasagne for dinner alongside a glass of wine. What is the most likely diagnosis?

Acute asthma attack	1%
Carcinoid syndrome	17%
Exercise induced wheat angioedema	50%
Shellfish anaphylaxis	31%
Thyrotoxicosis	0%

Exercised induced anaphylaxis is now well described and is most associated with wheat ingestion. The clinical manifestations usually occur around 10 minutes after exercise and follow a sequence of pruritus, widespread urticaria and then subsequently respiratory distress and vascular collapse. The condition usually resolves on stopping exercise and is managed in the same manner as anaphylaxis. The patients can usually eat the causative food without problems so long as they do not exercise afterwards. The physiology of the condition remains slightly unknown, but it may be related to endorphin release during exercise. The endocrines cause excessive histamine release from mast cells in susceptible individuals.

The tingling lips and facial flushing are not in keeping with an asthma attack and there is no history of shellfish consumption. Thyrotoxicosis could explain some of the symptoms but not the wheeze. Carcinoid syndrome can cause episodes of flushing, shortness of breath and tachycardia and thus represents a plausible option, especially as exercise, food and stress can trigger these episodes. However these patients often have diarrhoea and abdominal symptoms alongside their other symptoms.



Discuss (12)
Improve

Next question >

Anaphylaxis may be defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction.

Common identified causes of anaphylaxis:

- food (e.g. nuts) - the most common cause in children
- drugs
- venom (e.g. wasp sting)

Features

The Resus Council UK define anaphylaxis as:

- the sudden onset and rapid progression of symptoms
- **A**irway and/or **B**reathing and/or **C**irculation problems
- **A**irway problems may include:
 - swelling of the throat and tongue → hoarse voice and stridor
- **B**reathing problems may include:
 - respiratory wheeze
 - dyspnoea
- **C**irculation problems may include:
 - hypotension
 - tachycardia

This means that if there are no ABC problems then the patient is technically not having anaphylaxis.

Around 80-90% of patients also have skin and mucosal changes:

- generalised pruritus
- widespread erythematous or urticarial rash

Management

Anaphylaxis is one of the few times when you would not have time to look up the dose of a medication. The Resuscitation Council guidelines on anaphylaxis have recently been updated.

Intramuscular adrenaline is by far the most important drug in anaphylaxis and should be given as soon as possible. Previously IV hydrocortisone was also recommended but the evidence base for this was poor and it was removed in the 2021 update.

The recommended doses for adrenaline are as follows: **BNF**

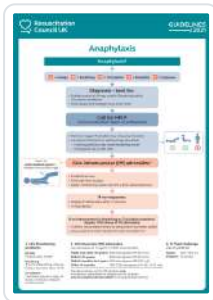
Age	Adrenaline dose
< 6 months	100 - 150 micrograms (0.1 - 0.15 ml 1 in 1,000)

Age	Adrenaline dose
6 months - 6 years	150 micrograms (0.15 ml 1 in 1,000)
6-12 years	300 micrograms (0.3ml 1 in 1,000)
Adult and child > 12 years	500 micrograms (0.5ml 1 in 1,000)

Adrenaline can be repeated every 5 minutes if necessary. The best site for IM injection is the anterolateral aspect of the middle third of the thigh.

Refractory anaphylaxis

- defined as respiratory and/or cardiovascular problems persist despite 2 doses of IM adrenaline
- IV fluids should be given for shock
- expert help should be sought for consideration of an IV adrenaline infusion



Management following stabilisation:

- non-sedating oral antihistamines, in preference to chlorphenamine, may be given following initial stabilisation especially in patients with persisting skin symptoms (urticaria and/or angioedema)
- sometimes it can be difficult to establish whether a patient had a true episode of anaphylaxis. Serum tryptase levels are sometimes taken in such patients as they remain elevated for up to 12 hours following an acute episode of anaphylaxis
- all patients with a new diagnosis of anaphylaxis should be referred to a specialist allergy clinic
- an adrenaline injector should be given as an interim measure before the specialist allergy assessment (unless the reaction was drug-induced)
 - patients should be prescribed 2 adrenaline auto-injectors
 - training should be provided on how to use it
- a risk-stratified approach to discharge should be taken as biphasic reactions can occur in up to 20% of patients

The Resus Council UK recommend the following risk-stratified approach to discharge:

- fast-track discharge (after 2 hours of symptom resolution):
 - good response to a single dose of adrenaline
 - complete resolution of symptoms
 - has been given an adrenaline auto-injector and trained how to use it

- adequate supervision following discharge
- minimum 6 hours after symptom resolution
 - 2 doses of IM adrenaline needed, or
 - previous biphasic reaction
- minimum 12 hours after symptom resolution
 - severe reaction requiring > 2 doses of IM adrenaline
 - patient has severe asthma
 - possibility of an ongoing reaction (e.g. slow-release medication)
 - patient presents late at night
 - patient in areas where access to emergency access care may be difficult
 - observation for at 12 hours following symptom resolution



123



Next question >

B

I



A



T



Textbooks

High-yield textbook

Extended textbook

Links

BNF



13



10

[Medical emergencies in the community](#)

Resus Council



31



8

[Anaphylaxis guidelines](#)

Clinical Knowledge Summaries



17



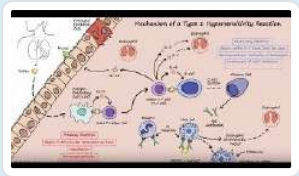
4

[Angio-oedema and anaphylaxis](#)



[Suggest link](#)

[Report broken link](#)

Media





Type I Hypersensitivity

PhysioPathoPharmaco - YouTube  3  2



Type I hypersensitivity

Osmosis - YouTube  1  1

[Report broken media](#)

Score: **13.9%**

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94	✓
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101	✗
102	-

A 54-year-old man presents to the emergency department with shortness of breath. He has a history of heart failure and takes ramipril, bisoprolol, eplerenone and isosorbide mononitrate.

Observations are as follows: heart rate 135 beats per minute, respiratory rate 26 breaths per minute, blood pressure 135/82 mmHg, temperature 37.4 °C, and SpO2 92%. His chest is clear on auscultation.

The doctors initiate the patient on 15L O2 via a non-rebreather mask.

Blood gas analysis results are as follows:

pH	7.24	(7.35 - 7.45)
PaO2	72.4 kPa	(10.3 - 13.3 kPa)
PaCO2	2.9 kPa	(4.7 - 6 kPa)
HCO3	16 mmol/L	(22 - 28 mmol/L)
SaO2	44%	(94 - 98%)
Lactate	3.4 mmol/L	(<1.0)

What is the most likely diagnosis?

- ☐
Acquired methaemoglobinaemia
×
- ☐
Carboxyhaemoglobinaemia
×
- ☐
Congenital methaemoglobinaemia
×
- ☐
Cyanide poisoning
×
- ☐
Pulmonary embolism
×

Submit answer

Reference ranges ▾

- | | |
|----|---|
| 1 | ✗ |
| 2 | ✗ |
| 3 | ✗ |
| 4 | ✗ |
| 5 | ✓ |
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| 9 | ✗ |
| 10 | ✗ |
| 11 | ✓ |
| 12 | ✗ |
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PaO2	72.4 kPa	(10.3 - 13.3 kPa)
PaCO2	2.9 kPa	(4.7 - 6 kPa)
HCO3	16 mmol/L	(22 - 28 mmol/L)
SaO2	44%	(94 - 98%)
Lactate	3.4 mmol/L	(<1.0)

What is the most likely diagnosis?

Acquired methaemoglobinaemia	79%
Carboxyhaemoglobinaemia	10%
Congenital methaemoglobinaemia	5%
Cyanide poisoning	5%
Pulmonary embolism	2%

Nitrates, including recreational nitrates such as amyl nitrite ('poppers') may cause methaemoglobinaemia

Important for me Less important

The striking feature, in this case, is the significant discrepancy between the PaO2 and SaO2 on arterial blood gas analysis.

Given the patient is on 15L O₂, the PaO₂ is at a level expected indicating that gas exchange at the level of the alveoli is not impaired. There are various formulas for predicting the expected PaO₂ for any given inspired O₂ concentration. The Advanced Life Support (ALS) guidelines suggest that the PaO₂ for any given inspired concentration should be approximately 10 less than the inspired concentration (%). For example, in this case, 15L O₂ is equivalent to approximately 80-85% so we would expect the PaO₂ to be around 70 kPa.

However, it is important to note that the SaO₂ (oxygen saturation of haemoglobin) is markedly low at 44% indicating impaired oxygen binding to haemoglobin. It is also important to note that the peripheral SpO₂ is 92% which is clearly discrepant with the SaO₂. The two main causes of this picture are methaemoglobinaemia and carboxyhaemoglobinaemia. Because standard pulse oximeters are not capable of differentiating between different forms of bound haemoglobin, the SpO₂ is usually falsely high in these conditions.

Tissue hypoxia can be a consequence of 4 main causes:

- 1. Hypoxaemia (low PaO₂ due to poor gas exchange at the alveoli)
- 2. Toxic haemoglobin (low SaO₂ due to methaemoglobinaemia or carboxyhaemoglobinaemia)
- 3. Perfusional (e.g. shock, or localised causes such as compartment syndrome or bowel ischaemia)
- 4. Severe anaemia

Regardless of the cause, tissue hypoxia will result in lactic acidosis. Therefore, in patients with lactic acidosis, all the aforementioned causes should be considered. The patient in this case most certainly has lactic acidosis as a consequence of toxic haemoglobin-induced tissue hypoxia. He is acidotic with low serum bicarbonate since this acts as a buffer for lactic acid.

Acquired methaemoglobinaemia is the correct answer. As discussed above, the biochemical results are suggestive of toxic haemoglobin. The history of isosorbide mononitrate use favours the diagnosis of acquired methaemoglobinaemia. Nitrate-containing drugs are commonly implicated in this condition.

Carboxyhaemoglobinaemia is incorrect. Although carbon monoxide poisoning presents similarly and remains within the differential diagnosis, the history of nitrate exposure favours the diagnosis of methaemoglobinaemia.

Congenital methaemoglobinaemia is incorrect. Although this remains within the differential diagnosis, the absence of previous episodes and the presence of a known risk factor (e.g. nitrate exposure) favours the acquired form.

Cyanide poisoning is incorrect. Cyanide binds the ferric (Fe³⁺) ion of cytochrome oxidase causing 'histotoxic hypoxia' and lactic acidosis. It would not cause a marked reduction of SaO₂ as seen in this case unless it was associated with coexistent carbon monoxide poisoning (e.g. due to smoke inhalation). There is nothing in this clinical case to suggest that this is the case.

Pulmonary embolism is incorrect. As stated above, the blood gas analysis confirms hypoxaemia

as a consequence of toxic haemoglobin rather than poor gas exchange at the level of the alveolar. Therefore a pulmonary embolism is a less likely diagnosis.



Discuss (2)

Improve

Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO_2 but decreased oxygen saturation

Management

- NADH methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



+

Q

123



Next question >

B

I



A



T





Textbooks

High-yield textbook

Extended textbook



Links

Life in the Fast Lane

 6  3

[Methaemoglobinaemia](#)

The Internet Book of Critical Care

 10  4

[Methemoglobinemia](#)



[Suggest link](#)

[Report broken link](#)

Media





[Methaemoglobinaemia](#)


Osmosis - YouTube  7  2


[Report broken media](#)

Score: **13.9%**

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101	✗
102	-



Question 81 of 191



A 75-year-old man presents to the emergency department with a reduced level of consciousness after a recent fall and head injury. He has a past medical history of atrial fibrillation. His medications include apixaban and bisoprolol.

On examination, his Glasgow coma scale is 12/15 (E 3 V4 M5). There is evidence of an external head injury with bruising and laceration in the right occipital area.

An urgent CT head is arranged, which demonstrates a large right-sided subdural haematoma.

What is the most appropriate medication to administer?

- | | | |
|-----------------------|---------------------|---|
| <input type="radio"/> | Andexanet alfa | × |
| <input type="radio"/> | Fresh frozen plasma | × |
| <input type="radio"/> | Vitamin K | × |
| <input type="radio"/> | Prothrombin complex | × |
| <input type="radio"/> | Idarucizumab | × |

Submit answer

Reference ranges 

Score: 12%

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| 1 | × |
| 2 | × |
| 3 | × |
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A 75-year-old man presents to the emergency department with a reduced level of consciousness after a recent fall and head injury. He has a past medical history of atrial fibrillation. His medications include apixaban and bisoprolol.

On examination, his Glasgow coma scale is 12/15 (E 3 V4 M5). There is evidence of an external head injury with bruising and laceration in the right occipital area.

An urgent CT head is arranged, which demonstrates a large right-sided subdural haematoma.

What is the most appropriate medication to administer?

Andexanet alfa	67%
Fresh frozen plasma	3%
Vitamin K	1%
Prothrombin complex	13%
Idarucizumab	15%

Rivaroxaban and apixaban can be reversed by andexanet alfa

Important for me Less important

Andexanet alfa is the correct answer. The patient has sustained a traumatic subdural haematoma. Clinically he has a low GCS. The method of anticoagulation needs to be reversed. The most appropriate reversal agent for apixaban is andexanet alfa.

Vitamin K is incorrect. This can be used as a reversal agent for warfarin. It is not the most appropriate agent to use given this patient's method of anticoagulation.

Fresh frozen plasma is incorrect. This is mainly used to replace coagulation factors in cases of excessive bleeding or in those with abnormal coagulation. It is not the most appropriate reversal agent available to choose in this case.

Prothrombin complex is incorrect. This can be used to rapidly reverse the effects of warfarin in those patients that are bleeding. It is under investigation currently to see if it is effective in reversing agents such as apixaban.

Idarucizumab is incorrect. This is a monoclonal antibody that can reverse the effects of dabigatran.



Discuss (5)

Improve

Next question >

Direct oral anticoagulants ★

Direct oral anticoagulants (DOACs) are currently used for the following indications:

- prevention of stroke in non-valvular AF. NICE stipulate that certain other risk factors should be present. These are complicated and differ between the DOACs but generally require one of the following to be present:
 - prior stroke or transient ischaemic attack
 - age 75 years or older
 - hypertension
 - diabetes mellitus
 - heart failure
- prevention of VTE following hip/knee surgery
- treatment of DVT and PE

The table below summaries some of the differences between the DOACs:

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Mechanism of action	Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Excretion	Majority renal	Majority liver	Majority faecal	Majority faecal
Reversal	Idarucizumab	Andexanet alfa*	Andexanet alfa*	No authorised reversal agent, although andexanet alfa has been studied

*Andexanet alfa is a recombinant form of human factor Xa protein



123



Next question >



Textbooks

High-yield textbook

Extended textbook



Links

Royal College of Physicians

 5  4

[Drug therapy in anticoagulation: which drug for which patient?](#)

NICE

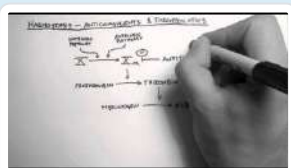
 6  3

[2012 Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation](#)



[Suggest link](#)

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Media





[Haemostasis 3 - Anticoagulants & Thrombolytics](#)

Handwritten Tutorials - YouTube  13  0



[Antiplatelets and anticoagulants made easy](#)

Speed Pharmacology - YouTube  2  0

[Report broken media](#)

Score: **13.9%**

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Question 82 of 191



You are looking after a 35-year-old man who is in the oncology day unit receiving his second round of chemotherapy for a low grade non-Hodgkin's lymphoma. His lymphoma is confined to two lymph node groups in his anterior cervical chain and right inguinal region. In total there are 6 nodes with the largest being 4cm in size. He had no issues during his first round of chemotherapy apart from some nausea a week afterwards. He has no other medical problems and is on no other medications. His bloods pre-chemotherapy are as shown below:

Na ⁺	137 mmol/l
K ⁺	3.8 mmol/l
Urea	2.8 mmol/l
Creatinine	55 µmol/l
Corrected Calcium	2.39 µmol/l
Phosphate	1.05 µmol/l

What regimen would be most appropriate for prevention of tumour lysis syndrome in his case?

- ☐ Allopurinol (200mg BD) ×
- ☐ Fluids and allopurinol (200mg BD) ×
- ☐ Fluids and rasburicase (0.2mg/kg) ×
- ☐ Reduced dose chemotherapy ×
- ☐ Fluids, allopurinol (200mg BD) and rasburicase (0.2mg/kg) ×

Submit answer

Reference ranges 

Score: 12%

1 ×

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82 -

You are looking after a 35-year-old man who is in the oncology day unit receiving his second round of chemotherapy for a low grade non-Hodgkin's lymphoma. His lymphoma is confined to two lymph node groups in his anterior cervical chain and right inguinal region. In total there are 6 nodes with the largest being 4cm in size. He had no issues during his first round of chemotherapy apart from some nausea a week afterwards. He has no other medical problems and is on no other medications. His bloods pre-chemotherapy are as shown below:

Na ⁺	137 mmol/l
K ⁺	3.8 mmol/l
Urea	2.8 mmol/l
Creatinine	55 µmol/l
Corrected Calcium	2.39 µmol/l
Phosphate	1.05 µmol/l

What regimen would be most appropriate for prevention of tumour lysis syndrome in his case?

Allopurinol (200mg BD)	5%
Fluids and allopurinol (200mg BD)	36%
Fluids and rasburicase (0.2mg/kg)	45%
Reduced dose chemotherapy	0%
Fluids, allopurinol (200mg BD) and rasburicase (0.2mg/kg)	13%

The British Society of Haematology suggest that patients undergoing chemotherapy can be categorised into three different risk groups for tumour lysis syndrome. While you are not required to know how to do this in detail it would be important clinically to be able to recognise factors that put people at increased risk:

- High tumour burden
- High grade tumours with rapid cell turnover
- Pre-existing renal impairment or renal involvement by the tumour
- Increased age
- Treatment with highly active, cell-cycle specific agents
- Concomitant use of drugs that increase uric acid levels (the list is available on the guidance)



Risk Group	Prophylaxis
Low Risk	Adequate hydration (consider IV fluids and allopurinol prophylaxis)
Intermediate Risk	Allopurinol (7 days) and IV fluids
High Risk	Rasburicase and IV fluids (consider low dose chemotherapy)


This patient has no high risk features in his history and is therefore considered low risk, so the closest answer is fluids and allopurinol.

It is important to know that allopurinol and rasburicase should not be used together, as allopurinol reduces the effectiveness of rasburicase. Allopurinol reduces the production of urate, allowing elimination of upstream compounds, which are more water soluble and thus more easy to excrete through the kidneys. Rasburicase, on the other hand, converts urate into more easily excreted downstream compounds.

In addition rasburicase cannot be given to patients with G6PD as it can precipitate haemolysis.

<http://onlinelibrary.wiley.com/doi/10.1111/bjh.13403/epdf>


 Discuss (5)

Improve

Next question >

Tumour lysis syndrome ★

Tumour lysis syndrome (TLS) is a potentially deadly condition related to the treatment of high-grade lymphomas and leukaemias. It can occur in the absence of chemotherapy but is usually triggered by the introduction of combination chemotherapy. On occasion, it can occur with steroid treatment alone. Awareness of the condition is critical as prophylactic medication can be given to prevent the potentially deadly effects of tumour cell lysis.

TLS occurs from the breakdown of the tumour cells and the subsequent release of chemicals from the cell. It leads to a high potassium and high phosphate level in the presence of a low calcium. It should be suspected in any patient presenting with an acute kidney injury in the presence of a high phosphate and high uric acid level.

Prevention

- IV fluids
- patients are higher risk should receive either allopurinol or rasburicase
- rasburicase

- a recombinant version of urate oxidase, an enzyme that metabolizes uric acid to allantoin. Allantoin is much more water-soluble than uric acid and is, therefore, more easily excreted by the kidneys
- generally preferred now for patients at a higher risk of developing TLS
- allopurinol
 - generally used for patients in lower-risk groups
- rasburicase and allopurinol should not be given together in the management of tumour lysis syndrome as this reduces the effect of rasburicase

From 2004 TLS has been graded using the Cairo-Bishop scoring system -

Laboratory tumor lysis syndrome: abnormality in two or more of the following, occurring within three days before or seven days after chemotherapy.

- uric acid > 475umol/l or 25% increase
- potassium > 6 mmol/l or 25% increase
- phosphate > 1.125mmol/l or 25% increase
- calcium < 1.75mmol/l or 25% decrease

Clinical tumor lysis syndrome: laboratory tumour lysis syndrome plus one or more of the following:

- increased serum creatinine (1.5 times upper limit of normal)
- cardiac arrhythmia or sudden death
- seizure



123



Next question >

B

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A



Textbooks



High-yield textbook

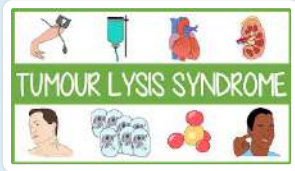
Extended textbook

Media





Tumour Lysis Syndrome

Oncology for Medical Students - YouTube  2  0





Tumour Lysis Syndrome in 3 Minutes

Townsend Teaching - YouTube  1  0



Tumour lysis syndrom

Armando Hasudungan - YouTube  5  1

[Report broken media](#)

Score: **13.9%**

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102	-



Question 83 of 191



A 24-year-old man is brought into the resuscitation room. They were struggling to walk across the emergency department reception area due to severe dyspnoea.

They admit to inhaling some substances at a party earlier in the evening but cannot recall what it was.

On examination, they have blue-tinged peripheries with blue lips and tip of nose but appear relatively undistressed. Their observations show oxygen saturations of 90% on 6 litres of oxygen and a heart rate of 120 beats per minute.

An arterial blood gas is taken while they are on 6 litres of oxygen. The results are below.

pH	7.40	(7.35-7.45)
paO2	18	(11-13)
paCO2	4.6	(4.5-6)
methaemoglobin	38%	(1-3%)

What is the most likely substance that they have ingested?

- ☐ Amyl nitrite ×
- ☐ Glyceryl trinitrate ×
- ☐ Sodium nitroprusside ×
- ☐ Aniline dye ×
- ☐ Dapsone ×

Submit answer

Reference ranges 

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| 8 | ✓ |
| 9 | ✗ |
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| 11 | ✓ |
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| 27 | ✗ |
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| 32 | ✓ |
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pH	7.40	(7.35-7.45)
paO2	18	(11-13)
paCO2	4.6	(4.5-6)
methaemoglobin	38%	(1-3%)

What is the most likely substance that they have ingested?

Amyl nitrite	70%
Glyceryl trinitrate	1%
Sodium nitroprusside	9%
Aniline dye	9%
Dapsone	10%

Nitrates, including recreational nitrates such as amyl nitrite ('poppers') may cause methaemoglobinaemia

Important for me Less important

The answer is amyl nitrite otherwise known as 'poppers' which is a drug of abuse. It induces a short lived euphoric high but can result in methaemoglobinaemia.

The other answers all cause methaemoglobinaemia but are unlikely to be used in the above context.



Discuss (4)

Improve

Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO_2 but decreased oxygen saturation

Management

- NADH methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



+

Q

123



Next question >

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A



T





Textbooks

High-yield textbook

Extended textbook



Links

Life in the Fast Lane

 6  3

[Methaemoglobinaemia](#)

The Internet Book of Critical Care

 10  4

[Methemoglobinemia](#)



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Media





[Methaemoglobinaemia](#)


Osmosis - YouTube  7  2


[Report broken media](#)

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Question 84 of 191



You are called to see a 55-year-old gentleman who is having a blood transfusion for symptomatic anaemia secondary to colon cancer. The nurses have been doing regular observations as documented below.

10am: Baseline observations prior to blood transfusion

Respiratory rate 20 breaths/min

Saturations 96% on air

Temperature 37.5 °c

Blood pressure 145/78 mmHg

Heart rate 74 beats/min

10:15 am: repeat observations after 15 mins of transfusion

Respiratory rate 19 breaths/min

Saturations 97% on air

Temperature 38.2 °c

Blood pressure 150/80 mmHg

Heart rate 72 beats/min

The nurses have already stopped the blood transfusion by the time you arrive to see the patient. On questioning the patient he feels well with no complaints of pain, itch or rashes. On examination his heart sounds are pure and chest is clear. He has no previous documented reactions to blood transfusions although the patient informs you he is allergic to penicillin. What instructions do you give the nurses?

- ☐ Take blood cultures and commence antibiotics ×
- ☐ Dispose of the remaining blood in the bag ×
- ☐ Restart the blood transfusion after giving the patient paracetamol ×
- ☐ Take blood cultures, repeat chest x ray and perform urinalysis ×
- ☐ Restart the blood transfusion an hour after giving the patient paracetamol ×

Submit answer

Score: **12%**

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You are called to see a 55-year-old gentleman who is having a blood transfusion for symptomatic anaemia secondary to colon cancer. The nurses have been doing regular observations as documented below.

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Respiratory rate 20 breaths/min

Saturations 96% on air

Temperature 37.5 °c

Blood pressure 145/78 mmHg

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10:15 am: repeat observations after 15 mins of transfusion

Respiratory rate 19 breaths/min

Saturations 97% on air

Temperature 38.2 °c

Blood pressure 150/80 mmHg

Heart rate 72 beats/min

The nurses have already stopped the blood transfusion by the time you arrive to see the patient. On questioning the patient he feels well with no complaints of pain, itch or rashes. On examination his heart sounds are pure and chest is clear. He has no previous documented reactions to blood transfusions although the patient informs you he is allergic to penicillin. What instructions do you give the nurses?

Take blood cultures and commence antibiotics	1%
Dispose of the remaining blood in the bag	3%
Restart the blood transfusion after giving the patient paracetamol	68%
Take blood cultures, repeat chest x ray and perform urinalysis	2%
Restart the blood transfusion an hour after giving the patient paracetamol	26%

Blood transfusion reaction are common and can be serious. This patient is well and has no clinical evidence of haemodynamic compromise. He has an isolated pyrexia which is likely to be secondary to commencement of the blood transfusion. After confirming this his blood transfusion should be restarted as soon as possible and paracetamol given for symptomatic relief. Disposal of the blood

should be considered if a serious adverse reaction occurs. Septic screen and antibiotics should be considered if any underlying infection is suspected. Blood transfusion should be completed within 4 hours and waiting an hour prior to restarting is a waste of valuable time.



Discuss (2)

Improve

Next question >

Blood product transfusion complications ★

Blood product transfusion complications may be broadly classified into the following:

- immunological: acute haemolytic, non-haemolytic febrile, allergic/anaphylaxis
- infective
- transfusion-related acute lung injury (TRALI)
- transfusion-associated circulatory overload (TACO)
- other: hyperkalaemia, iron overload, clotting

The table below summaries some of the key features:

Reaction	Features	Management
Non-haemolytic febrile reaction Thought to be caused by antibodies reacting with white cell fragments in the blood product and cytokines that have leaked from the blood cell during storage	Fever, chills Red cell transfusion (1-2%) Platelet transfusion (10-30%)	Slow or stop the transfusion Paracetamol Monitor
Minor allergic reaction Thought to be caused by foreign plasma proteins	Pruritus, urticaria	Temporarily stop the transfusion Antihistamine Monitor
Anaphylaxis Can be caused by patients with IgA deficiency who have anti-IgA antibodies	Hypotension, dyspnoea, wheezing, angioedema.	Stop the transfusion IM adrenaline ABC support <ul style="list-style-type: none">• oxygen• fluids

Reaction	Features	Management
<u>Acute haemolytic reaction</u> ABO-incompatible blood e.g. secondary to human error	Fever, abdominal pain, hypotension	Stop transfusion Confirm diagnosis <ul style="list-style-type: none"> • check the identity of patient/name on blood product • send blood for direct Coombs test, repeat typing and cross-matching Supportive care <ul style="list-style-type: none"> • fluid resuscitation
Transfusion-associated circulatory overload (TACO) Excessive rate of transfusion, pre-existing heart failure	Pulmonary oedema, hypertension	Slow or stop transfusion Consider intravenous loop diuretic (e.g. furosemide) and oxygen
Transfusion-related acute lung injury (TRALI) Non-cardiogenic pulmonary oedema thought to be secondary to increased vascular permeability caused by host neutrophils that become activated by substances in donated blood	Hypoxia, pulmonary infiltrates on chest x-ray, fever, hypotension	Stop the transfusion Oxygen and supportive care

Further information is provided below:

Acute haemolytic transfusion reaction

Acute haemolytic transfusion reaction results from a mismatch of blood group (ABO) which causes massive intravascular haemolysis. This is usually the result of red blood cell destruction by IgM-type antibodies.

Symptoms begin minutes after the transfusion is started and include a fever, abdominal and chest pain, agitation and hypotension.

Treatment should include immediate transfusion termination, generous fluid resuscitation with saline solution and informing the lab

Complications include disseminated intravascular coagulation, and renal failure

Non-haemolytic febrile reaction

Febrile reactions

- due to white blood cell HLA antibodies
- often the result of sensitization by previous pregnancies or transfusions
- paracetamol may be given

Allergic/anaphylaxis reaction

Allergic reactions to blood transfusions are caused by hypersensitivity reactions to components within the transfusion. Symptoms typically arise within minutes of starting the transfusion and severity can range from urticaria to anaphylaxis with hypotension, dyspnoea, wheezing, and stridor, or angioedema.

Simple urticaria should be treated by discontinuing the transfusion and with an antihistamine. Once the symptoms resolve, the transfusion may be continued with no need for further workup.

More severe allergic reaction or anaphylaxis should be treated urgently. The transfusion should be permanently discontinued, intramuscular adrenaline should be administered and supportive care. Antihistamine, corticosteroids and bronchodilators should also be considered for these patients.

Transfusion-related acute lung injury (TRALI)

A rare but potentially fatal complication of blood transfusion. Characterised by the development of hypoxaemia / acute respiratory distress syndrome within 6 hours of transfusion. Features include:

- hypoxia
- pulmonary infiltrates on chest x-ray
- fever
- hypotension

Transfusion-associated circulatory overload (TACO)

A relatively common reaction due to fluid overload resulting in pulmonary oedema. As well as features of pulmonary oedema the patient may also be hypertensive, a key difference from patients with TRALI.

Infective

Bacterial and viral

The risk of infectious complications varies with different types of blood products due to their storage conditions, components involved, and duration of storage.

Red Blood Cells (RBCs)

- Pathogens: RBCs are primarily at risk for transmitting viral agents such as HIV, HBV, and HCV. Bacterial contamination is less common but possible, particularly from skin flora during collection.
- Clinical impact: Viral infections can lead to chronic disease states such as chronic hepatitis or AIDS. Bacterial infections may manifest as sepsis if not promptly treated.

Platelets

- Pathogens: Platelets are stored at room temperature, which increases the risk of bacterial proliferation. Common contaminants include *Staphylococcus epidermidis* and *Bacillus cereus*.
- Clinical impact: Bacterial contamination of platelets is more likely to lead to rapid onset of sepsis and septic shock, given the optimal growth conditions during storage.

Prions

Transmission of vCJD

- although the absolute risk is very small, vCJD may be transmitted via blood transfusion
- a number of steps have been taken to minimise this risk, including:
 - from late 1999 onward, all donations have undergone removal of white cells (leucodepletion) in order to reduce any vCJD infectivity present
 - from 1999, plasma derivatives have been fractionated from imported plasma rather than being sourced from UK donors. Fresh Frozen Plasma (FFP) used for children and certain groups of adults needing frequent transfusions is also imported
 - from 2004 onward, recipients of blood components have been excluded from donating blood



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Links

Serious Hazards of Tranfusion

 6  16



[SHOT website](#)

Gov.uk

 6  11

[2013 vCJD and Transfusion of Blood Components: an Updated Risk Assessment](#)

British Journal of Haematology

 11  14

[Algorithm for managing an acute transfusion reaction](#)

[Suggest link](#)



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Media




[Blood transfusion reactions and transplant rejection](#)


Osmosis - YouTube


 3  1

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Question 85 of 191



A 55-year-old lady presents to her general practitioner with a painful rash on her breasts. The rash has developed over the last 24 hours and although initially diffuse and red is now well demarcated and a much darker red. She was started on warfarin five days ago for a deep vein thrombosis diagnosed on ultrasound doppler. She has a past medical history of hypothyroidism, type two diabetes mellitus, thromboembolism and obesity. She remembers having been on warfarin at least once before for previous deep vein thrombosis but does not remember ever having had this rash. Her blood tests today are as follows.

Prothrombin time	21.4 seconds
INR	2.1 ratio

What is the most likely diagnosis?

- ☐ Protein S deficiency ×
- ☐ Idiosyncratic drug reaction ×
- ☐ Stevens Johnson syndrome ×
- ☐ Warfarin toxicity ×
- ☐ Protein C deficiency ×

Submit answer

Reference ranges 

Score: **12%**

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A 55-year-old lady presents to her general practitioner with a painful rash on her breasts. The rash has developed over the last 24 hours and although initially diffuse and red is now well demarcated and a much darker red. She was started on warfarin five days ago for a deep vein thrombosis diagnosed on ultrasound doppler. She has a past medical history of hypothyroidism, type two diabetes mellitus, thromboembolism and obesity. She remembers having been on warfarin at least once before for previous deep vein thrombosis but does not remember ever having had this rash. Her blood tests today are as follows.

Prothrombin time	21.4 seconds
INR	2.1 ratio

What is the most likely diagnosis?

Protein S deficiency	8%
Idiosyncratic drug reaction	18%
Stevens Johnson syndrome	3%
Warfarin toxicity	10%
Protein C deficiency	61%

Warfarin-induced skin necrosis is a symptom of the hypercoagulable state that can be seen in the first week of warfarin therapy. This is explained by the fact that warfarin inhibits both pro-coagulant factors (2, 7, 9, 10) as well as anti-coagulant factors (protein C). Protein C has the shortest half-life and therefore there is a short period of time during the initiation of warfarin therapy where the patient is hypercoagulable despite a therapeutic INR. Warfarin-induced skin necrosis is more likely to occur in patients with pre-existing protein C deficiency, which is a rare congenital condition associated with recurrent venous thromboembolic disease.





 Discuss (9)

 Improve

Next question >

Protein C deficiency ★

Protein C deficiency is an autosomal codominant condition which causes an increased risk of thrombosis

Features

- venous thromboembolism
- skin necrosis following the commencement of warfarin: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis

 + Q 123 

Next question >

B


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Textbooks

High-yield textbook

Extended textbook


Links

Rare Disease Video Library - NORD

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[Protein C and Protein S Deficiency](#)

DermnetNZ

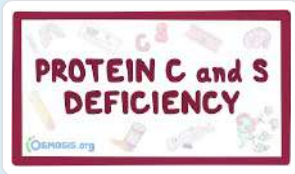
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[Warfarin induced skin necrosis](#)



Suggest link

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Media



Protein C and S deficiency

Osmosis - YouTube  4  0

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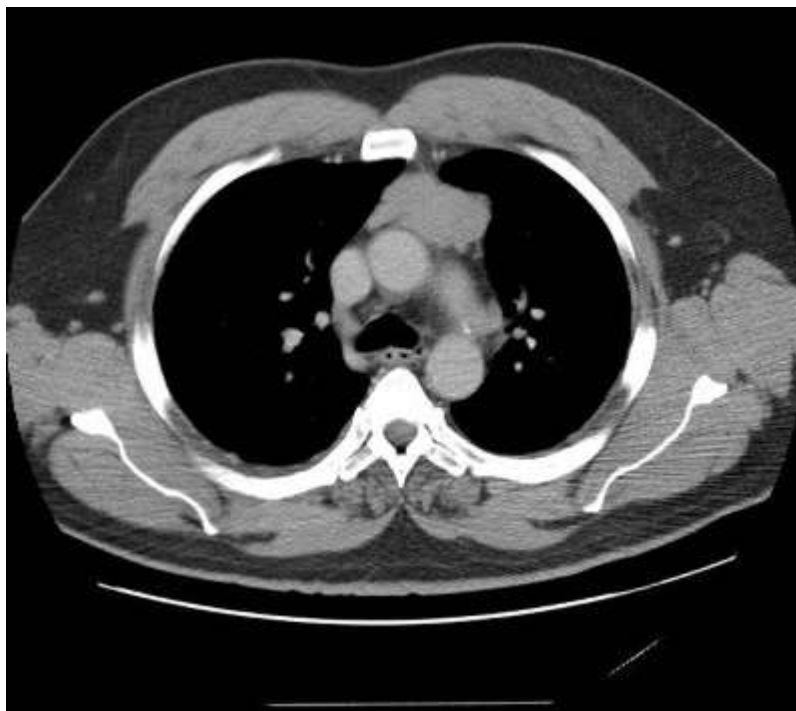


Question 86 of 191



A 41-year-old woman presents to her general practitioner with a three-month history of shortness of breath and cough. Her symptoms have been progressive and she is otherwise asymptomatic. She has no relevant medical comorbidities but a 30 pack-year smoking history.

Examination of the respiratory systems is unremarkable. She has a CT thorax which is displayed below:



© Image used on license from Radiopaedia



What is the most likely cause for this woman's symptoms?

- ☐ Bronchial cancer ×
- ☐ Chronic pulmonary emboli ×
- ☐ Lung fibrosis ×
- ☐ Thymoma ×
- ☐ Thyroid cancer ×

Submit answer

Score: **12%**

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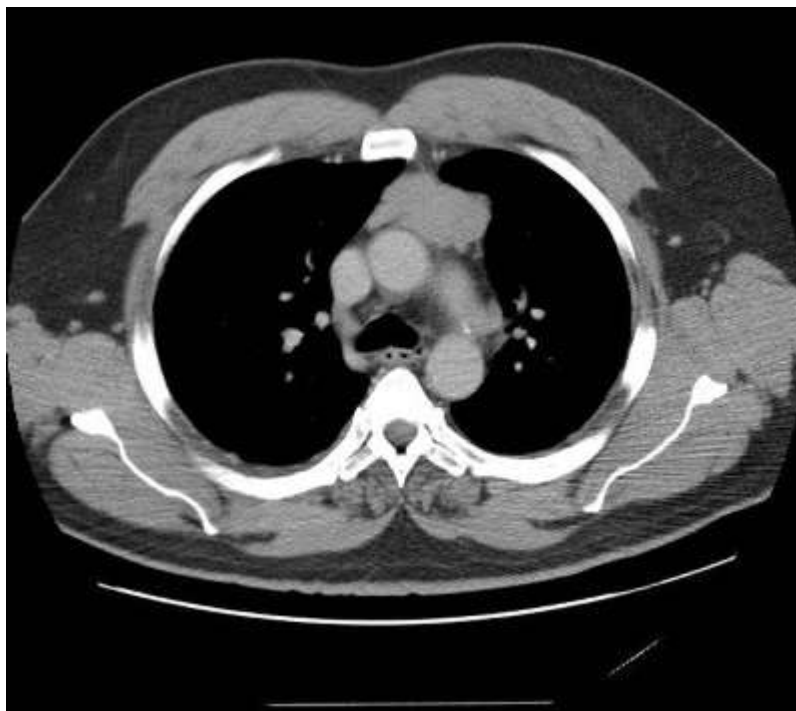
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Examination of the respiratory systems is unremarkable. She has a CT thorax which is displayed below:



© Image used on license from Radiopaedia



What is the most likely cause for this woman's symptoms?

Bronchial cancer	11%
Chronic pulmonary emboli	12%
Lung fibrosis	1%
Thymoma	74%
Thyroid cancer	2%


This woman's CT scan demonstrates a large mass representing a thymoma in the anterior mediastinum. Thymomas can commonly cause shortness of breath and cough, as well as retrosternal chest pain, dysphagia, and vocal changes.

Although bronchial cancer could cause this woman's symptoms, there is no evidence of this pathology on the CT and therefore this answer is incorrect.

There is no evidence on this CT scan of a pulmonary embolus despite this not being a pulmonary angiogram. As the scan does identify a thymoma, chronic pulmonary emboli are therefore less likely and incorrect.

Although not a high-resolution scan, there is no evidence of fibrosis within the lung fields and therefore this answer is incorrect.

The anterior mediastinal mass shown on this CT scan is too inferior to be a thyroid cancer which would typically present as a lump in the neck. Therefore the diagnosis of thymoma is more likely and thyroid cancer is incorrect.

Discuss (3)

Improve

Next question >

Thymoma ★

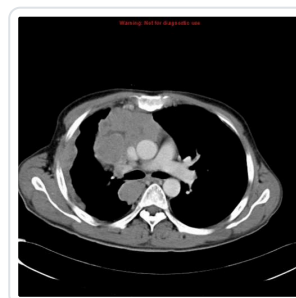
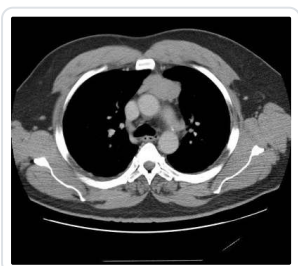
Thymomas are the most common tumour of the anterior mediastinum and is usually detected between the sixth and seventh decades of life.

Associated with

- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death

- compression of airway
- cardiac tamponade



123



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Textbooks

High-yield textbook

Extended textbook

Links

Radiopaedia

8
 3

Thymic tumours

Suggest link

Report broken link

Score: **13.9%**

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100	✗
101	✗
102	-

A 64-year-old woman presents to her general practitioner with a one-day history of swollen left leg associated with pain. She has a past medical history of heart failure and hypertension and takes bisoprolol, ramipril, amlodipine, and furosemide. She is significantly limited in her mobility.

On examination, the left calf is red and 4cm larger than the right. There is tenderness over the deep venous system. There is bilateral, symmetrical pedal oedema. The left thigh is unremarkable.

2-level DVT Wells test

Criteria	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2



What is the most appropriate next step?

- ☐ CT pulmonary angiogram ×
- ☐ D-dimer ×
- ☐ Inferior vena cava filter ×
- ☐ Lower limb venous ultrasound ×
- ☐ VQ scan ×

Submit answer

Score: 12%

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2-level DVT Wells test

Criteria	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
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Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

What is the most appropriate next step?

CT pulmonary angiogram	6%
D-dimer	16%
Inferior vena cava filter	1%
Lower limb venous ultrasound	77%
VQ scan	0%

This woman has a 2-level Wells' score of 2 (calf swelling, tenderness over the deep venous system) for deep vein thrombosis (DVT). NICE guidance states that a score of 2 or above should be investigated by **lower limb venous ultrasound** rather than high sensitivity d-dimer testing.

CT pulmonary angiography (CTPA) could be considered to check for a pulmonary embolus (PE) once a DVT is confirmed however this is not indicated at this stage.

High-sensitivity **d-dimer** testing is the first-line investigation for patients who have a 2-level Wells' score of less than 2. As this patient scores 2, a lower limb ultrasound should be performed and therefore this is an incorrect answer.

An **inferior vena cava filter** is a treatment for DVT, particularly in cases where anticoagulation is not an option. As a DVT has not been confirmed, this would not be the most appropriate next step.

A **VQ scan** is an alternative imaging modality to CTPA for PE however as previously discussed, prior to confirmation of a DVT and with no clinical indication, this test would not be indicated at this stage.

   Discuss (1) [Improve](#)

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Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1

Clinical feature	Points
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)
 - interim therapeutic anticoagulation used to mean giving low-molecular weight heparin
 - NICE updated their guidance in 2020. They now recommend using an anticoagulant that can be continued if the result is positive.
 - this means normally a direct oral anticoagulant (DOAC) such as apixaban or rivaroxaban
- if the scan is negative but the D-dimer is positive:
 - stop interim therapeutic anticoagulation
 - offer a repeat proximal leg vein ultrasound scan 6 to 8 days later

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test
 - this should be done within 4 hours. If not, interim therapeutic anticoagulation should be given until the result is available
 - if the result is negative then DVT is unlikely and alternative diagnoses should be considered
 - if the result is positive then a proximal leg vein ultrasound scan should be carried out within 4 hours

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer

at increased risk

- an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



123



Next question >

B

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T



Textbooks

High-yield textbook

Extended textbook

Links

NICE



25



9

[2020 Venous thromboembolism guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



Deep vein thrombosis

Osmosis - YouTube

👍 3 👎 0



Understanding Deep Vein Thrombosis (DVT)

Zero To Finals - YouTube

👍 2 👎 1



Deep Vein Thrombosis - Overview (pathophysiology, treatment, complications)

Armando Hasudungan - YouTube

👍 3 👎 2

[Report broken media](#)

Score: **13.9%**

- 1 ✗
- 2 ✗
- 3 ✗
- 4 ✗
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- 6 ✗
- 7 ✗
- 8 ✓
- 9 ✗
- 10 ✗
- 11 ✓
- 12 ✗
- 13 ✗

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Question 88 of 191



A 19-year-old man presents to your clinic. For as long as he can remember, he has had a dusky discolouration that is not in keeping with the skin colour of any of his relatives, and he feels that it is becoming gradually duskier with time. He tells you that. The only medication he is taking is oral isotretinoin, for acne, which he has been taking on-and-off for four years. Auscultation of his chest was unremarkable. Oxygen saturation by pulse oximetry showed saturation of 91% and an arterial blood gas was done which showed a pO₂ of 10.6kPa, FO₂Hb of 65% and metHb of 30%.

What is the most appropriate treatment for this man?

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| <input type="radio"/> | Ascorbic acid | × |
| <input type="radio"/> | Corticosteroids | × |
| <input type="radio"/> | Methylene blue | × |
| <input type="radio"/> | Nocturnal CPAP | × |
| <input type="radio"/> | Vitamin A | × |

Submit answer

Reference ranges ▾

Score: 12%

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A 24 year-old medical student of Italian extraction returns from elective in India. One week after his return he presents with fever, headache, and myalgia.

Investigations are as follows:

Hb	10.1 g/dl
MCV	101.2 fl
Platelets	43 x10 ⁹ /l
WCC	6.1 x10 ⁹ /l
Na	134mmol/l
K	4.6 mmol/l
Urea	3.8 mmol/l
Creatinine	80 mol/l
ALT	44 IU/l
ALP	78 IU/l
Bilirubin	33 mol/l
Albumin	38 g/l
Thick and thin blood films	Plasmodium ovale parasites with red cells

What other blood test will be essential for the management of this condition?

- ☐ Coomb's test ×
- ☐ G6PD enzyme assay ×
- ☐ Chloroquine resistance test ×
- ☐ Ham's test ×
- ☐ Reticuloctye count ×

Submit answer

Score: **12%**

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What is the most appropriate treatment for this man?

Ascorbic acid	51%
Corticosteroids	0%
Methylene blue	46%
Nocturnal CPAP	1%
Vitamin A	2%

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency

Important for me Less important

This young man has methaemoglobinaemia. Methaemoglobin is an oxidised form of haemoglobin, where the iron of one of the subunits is in the ferric state (3+) and cannot, therefore, bind oxygen. Methaemoglobin occurs naturally (1% of total haemoglobin), but levels are regulated by NADH methaemoglobin reductase (cytochrome B5 reductase), which transfers electrons from NADH to methaemoglobin, converting methaemoglobin to haemoglobin. In methaemoglobinaemia, increased levels of methaemoglobin are seen.

The normal pO₂, with decreased FO₂Hb, indicates that the haemoglobin is not taking up the available oxygen. Pulse oximetry is less good at detecting hypoxia due to methaemoglobinaemia, as it relies somewhat on the assumption that haemoglobin is either oxygenated or deoxygenated and the fact that these forms absorb light of different wavelengths (940 or 660nm) to different extents. The presence of methaemoglobinaemia skews the ratio of absorbed light.

Methaemoglobinaemia may be acquired or congenital. There is no indication here that there is an acute cause such as medication or exposure to oxidising chemicals such as aniline dyes. Isotretinoin does not cause methaemoglobinaemia. This young man seems to have been suffering

from these symptoms for a while, and it is, therefore, more likely to be congenital methaemoglobinaemia, which is an autosomal recessive disorder characterised by the poor synthesis of methaemoglobin reductase.

There are two types of congenital methaemoglobinaemia. In type 1 methaemoglobin reductase is absent only in RBCs. This is associated with metHb levels of 10-35% and typically patients have a normal life expectancy, and may have cyanosis, but are otherwise asymptomatic, with fatigue and dyspnoea being the most commonly reported symptoms. In type 2, the enzyme is absent in all cells. This is associated with metHb levels >35%, causing developmental delay and severe neurological symptoms which are usually fatal in the first year of life.

Vitamin C (ascorbic acid) is the treatment for congenital methaemoglobinaemia, and one might expect his cyanosis to resolve within the proceeding few weeks.

Methylene blue would be the treatment if we were considering an acquired cause, but as explained above this is less likely.

Vitamin A, corticosteroids, and nocturnal CPAP play no role in the management of methaemoglobinaemia.



Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO₂ but decreased oxygen saturation

Management

- NADH methaemoglobinemia reductase deficiency: ascorbic acid
- IV methylnthioninium chloride (methylene blue) if acquired



123



Next question >

B

I



A



T



Textbooks

High-yield textbook

Extended textbook

Links

Life in the Fast Lane



6



3

[Methaemoglobinemia](#)

The Internet Book of Critical Care



10



4

[Methemoglobinemia](#)



[Suggest link](#)

[Report broken link](#)

Media



Methaemoglobinaemia

Osmosis - YouTube  7  2

[Report broken media](#)

Score: **13.9%**

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101	✗

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ALT	44 IU/l
ALP	78 IU/l
Bilirubin	33 mol/l
Albumin	38 g/l
Thick and thin blood films	Plasmodium ovale parasites with red cells

What other blood test will be essential for the management of this condition?

Coomb's test	6%
G6PD enzyme assay	65%
Chloroquine resistance test	20%
Ham's test	2%
Reticuloctye count	7%

The life cycle of *Plasmodium ovale* includes a dormant phase of liver hypnozoites, which may give rise to a new wave of parasitaemia after conventional treatment which targets only erythrocytic forms. Eradication of liver hypnozoites with primaquine is essential to prevent delayed relapse of infection.


Primaquine can precipitate haemolysis in individuals with G6PD (glucose-6-phosphate dehydrogenase) deficiency. G6PD activity should be tested before commencing treatment. If deficient, expert advice should be sought.

Coomb's test, also known as the direct antiglobulin test (DAT), detects antibody bound to the surface of red cells and is a test for autoimmune haemolytic anaemia. A variable degree of haemolysis occurs in malaria, but is not typically autoimmune. Rather it is due predominantly to destruction of infected red cells during parasite replication and breakdown in the spleen.

Chloroquine is the first-line treatment for non-falciparum malaria. Chloroquine resistance in *Plasmodium ovale* and *malariae* is extremely rare, but has been reported for vivax. Chloroquine is inadequate for the treatment of falciparum malaria as resistance is widespread.

Ham's test was previously used for the diagnosis of paroxysmal nocturnal haemoglobinuria, a condition which causes intravascular haemolysis.

Reticulocytes are red cell precursors, which are prematurely released from the marrow in response to haemolysis. Their large size accounts for the macrocytosis which often accompanies haemolytic anaemia. An elevated reticulocyte count is an appropriate response to haemolysis in the presence of an adequately functioning bone marrow.

   Discuss (9) [Improve](#)

[Next question >](#)

G6PD deficiency ★

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in an X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

Pathophysiology

- G6PD is the first step in the pentose phosphate pathway, which converts glucose-6-phosphate → 6-phosphogluconolactone
 - this reaction also results in nicotinamide adenine dinucleotide phosphate (NADP) → NADPH
 - i.e. $\text{glucose-6-phosphate} + \text{NADP} \rightarrow \text{6-phosphogluconolactone} + \text{NADPH}$
- NADPH is important for converting oxidized glutathione back to its reduced form
- reduced glutathione protects red blood cells from oxidative damage by oxidants such as superoxide anion (O_2^-) and hydrogen peroxide
- $\downarrow \text{G6PD} \rightarrow \downarrow \text{reduced NADPH} \rightarrow \downarrow \text{reduced glutathione} \rightarrow \text{increased red cell susceptibility to oxidative stress}$

Features

- neonatal jaundice is often seen
- intravascular haemolysis
- gallstones are common
- splenomegaly may be present
- Heinz bodies on blood films. Bite and blister cells may also be seen

Diagnosis is made by using a G6PD enzyme assay

- levels should be checked around 3 months after an acute episode of hemolysis, RBCs with the most severely reduced G6PD activity will have hemolysed → reduced G6PD activity → not be measured in the assay → false negative results

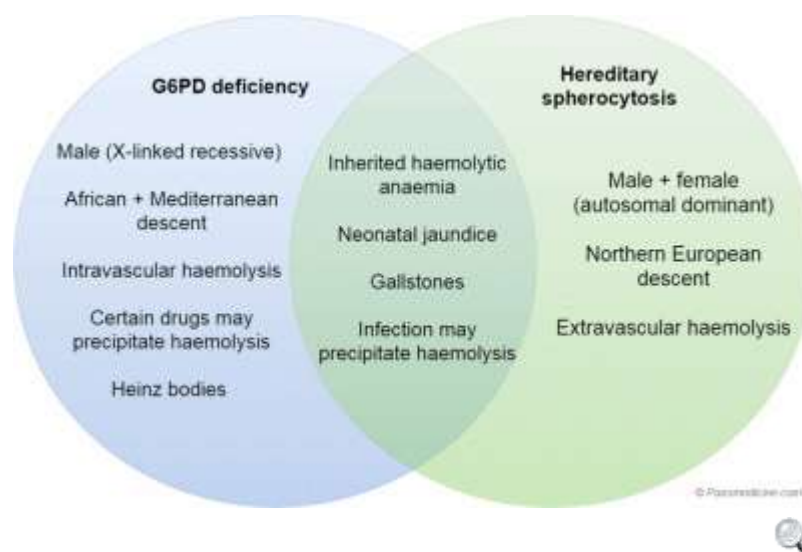
Some drugs causing haemolysis

- anti-malarials: primaquine
- ciprofloxacin
- sulph- group drugs: sulphonamides, sulphasalazine, sulfonylureas

Some drugs thought to be safe

- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

Comparing G6PD deficiency to hereditary spherocytosis:



Comparison of G6PD deficiency to hereditary spherocytosis

	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent
Typical history	<ul style="list-style-type: none"> • Neonatal jaundice • Infection/drugs precipitate haemolysis • Gallstones 	<ul style="list-style-type: none"> • Neonatal jaundice • Chronic symptoms although haemolytic crises may be precipitated by infection • Gallstones • Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	EMA binding



+

Q

123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Media

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

Osmosis - YouTube

7
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Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

Medicosis Perfectionalis - YouTube

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[Report broken media](#)

Score: **13.9%**

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Question 90 of 191



A 61-year-old woman comes for review. Around one year ago she finished a 6 month course of warfarin after being diagnosed with an unprovoked, proximal deep vein thrombosis. For the past few weeks she has been experiencing 'heaviness' and 'aching' in the the same leg. This is associated with an itch and some swelling, although this seems to go down each night. Past medical history of note includes osteoarthritis and type 2 diabetes mellitus.

On examination prominent varicose veins are seen on the affected leg with some brown discolouration of the skin above the medial malleolus. There is no difference in the circumference of the calves. Her temperature is 36.9°C, pulse 78/min and blood pressure 108/82 mmHg. What is the most likely diagnosis?

- | | | |
|-----------------------|------------------------------------|---|
| <input type="radio"/> | Recurrence of deep vein thrombosis | × |
| <input type="radio"/> | Post-thrombotic syndrome | × |
| <input type="radio"/> | Cellulitis | × |
| <input type="radio"/> | Ruptured Baker's cyst | × |
| <input type="radio"/> | Necrobiosis lipoidica | × |

Submit answer

Reference ranges 

Score: **12%**

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A 61-year-old woman comes for review. Around one year ago she finished a 6 month course of warfarin after being diagnosed with an unprovoked, proximal deep vein thrombosis. For the past few weeks she has been experiencing 'heaviness' and 'aching' in the the same leg. This is associated with an itch and some swelling, although this seems to go down each night. Past medical history of note includes osteoarthritis and type 2 diabetes mellitus.

On examination prominent varicose veins are seen on the affected leg with some brown discolouration of the skin above the medial malleolus. There is no difference in the circumference of the calves. Her temperature is 36.9°C, pulse 78/min and blood pressure 108/82 mmHg. What is the most likely diagnosis?

Recurrence of deep vein thrombosis	4%
Post-thrombotic syndrome	73%
Cellulitis	2%
Ruptured Baker's cyst	2%
Necrobiosis lipoidica	20%

Post-thrombotic syndrome is the correct diagnosis. This chronic condition develops in approximately 20-50% of patients following deep vein thrombosis (DVT) and typically presents with symptoms including leg heaviness, aching, pruritis, and oedema that improves with elevation (such as overnight). The presence of varicose veins and skin changes (particularly brown discolouration or hyperpigmentation) above the medial malleolus are classical signs. The pathophysiology involves damage to venous valves during the initial DVT, leading to chronic venous insufficiency.


Recurrence of DVT would be less likely in this case. While unprovoked DVT does carry a higher risk of recurrence, the clinical features are different. Acute DVT typically presents with more significant unilateral leg swelling, warmth, and tenderness. The improvement in symptoms overnight and chronic skin changes point away from acute DVT.


Cellulitis can be excluded based on the presentation. Cellulitis typically presents with acute onset erythema, warmth, tenderness, and often systemic symptoms such as fever. The patient's normal temperature and chronic nature of symptoms make this diagnosis unlikely.


Ruptured Baker's cyst typically presents with acute calf pain and swelling, often following activity. The pain is usually localised to the popliteal fossa and posterior calf. The chronic nature of

symptoms and venous changes make this diagnosis unlikely.

Necrobiosis lipoidica is a rare condition associated with diabetes mellitus that presents with well-demarcated, waxy, atrophic plaques, typically on the anterior shin. While this patient does have diabetes, her presentation with venous symptoms and characteristic post-thrombotic changes makes necrobiosis lipoidica an unlikely diagnosis.





 Discuss (2)

Improve

[Next question >](#)

Post-thrombotic syndrome ★








It is increasingly recognised that patients may develop complications following a DVT. Venous outflow obstruction and venous insufficiency result in chronic venous hypertension. The resulting clinical syndrome is known as post-thrombotic syndrome. The following features maybe seen:

- painful, heavy calves
- pruritus
- swelling
- varicose veins
- venous ulceration

Compression stockings have in the past been offered to patients with deep vein thrombosis to help reduce the risk of post-thrombotic syndrome. This is now not recommended.

However, once post-thrombotic syndrome has developed compression stockings are a recommended treatment. Other recommendations including keeping the leg elevated.

[Next question >](#)

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Textbooks

High-yield textbook

Extended textbook

Score: **13.9%**

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A 62-year-old gentleman with a background of Rheumatoid Arthritis, on maintenance sulfasalazine, is referred to the medical take from his GP with severe unremitting flu-like symptoms and deranged blood tests.

On examination, his temperature is 38.3 degrees celsius, heart rate 104bpm, respiratory rate 31/min and oxygen saturations 92% on room air.

His blood test reveals the following:

Hb	82 g/l
Platelets	$52 \times 10^9/l$
WBC	$18 \times 10^9/l$
Ferritin	50,000ng/ml
EBV Monospot test +ve	

He is initially treated as neutropaenic sepsis, with broad spectrum antimicrobials, and transferred to the intensive care unit for organ support. Unfortunately, he does not make any improvement. He is then seen by haematology who organise a bone marrow aspirate, revealing haemophagocytosis. What is the most likely underlying diagnosis?

- ☐ Macrophage activation syndrome ×
- ☐ Drug-induced pancytopenia ×
- ☐ Atypical infection ×
- ☐ Parvovirus infection ×
- ☐ Felty syndrome ×

Submit answer

Reference ranges 

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EBV Monospot test +ve	

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Macrophage activation syndrome	65%
Drug-induced pancytopenia	4%
Atypical infection	3%
Parvovirus infection	12%
Felty syndrome	16%

Macrophage activation syndrome is a condition characterised by excessive immune stimulation and cytokine storm in a rheumatological patient with an intercurrent EBV infection.

There is no suggestion in the question that there is a parvovirus infection and Felty syndrome would be characterised by a neutropaenia and splenomegaly. Drug-induced pancytopenia and atypical infections would not commonly show haemophagocytosis in the bone marrow.

Next question >

Macrophage activation syndrome ★

Macrophage activation syndrome is a rare disorder that is associated with rheumatological conditions such as juvenile idiopathic arthritis, rheumatoid arthritis or systemic lupus erythematosus. It commonly presents with a pancytopenia and intercurrent infection - particularly EBV - and is usually initially treated as neutropaenic sepsis.

Left untreated, the disease is often fatal after two months.


- Diagnosis: bone marrow aspiration can reveal haemophagocytosis as the key feature.
- Other features: excessive hyperferritinemia, elevated triglycerides, deranged LFTs, and hypofibrinogenemia.
- Treatment: immunosuppression.

 + Q 123 


Next question >

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Textbooks

High-yield textbook

Extended textbook

Score: **13.9%**

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Question 92 of 191



A 45-year-old woman is reviewed shortly after being diagnosed with having a pulmonary embolism. Around two weeks ago she was admitted with a severe community-acquired pneumonia which resulted in her being ventilated and admitted to ITU. She responded well to intravenous antibiotics but shortly before discharge became more short-of-breath again. A CTPA was requested which showed a pulmonary embolism. She is started immediately on dalteparin. What is the most appropriate next step?

- ☐ Stop dalteparin. Start a direct oral anticoagulant for 6 weeks ×
- ☐ Stop dalteparin. Start a direct oral anticoagulant for 3 months ×
- ☐ Stop dalteparin. Start a direct oral anticoagulant for 6 months ×
- ☐ Keep on dalteparin for 6 weeks ×
- ☐ Keep on dalteparin for 3 months ×

Submit answer

Reference ranges 

Score: **12%**

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Stop dalteparin. Start a direct oral anticoagulant for 6 weeks	2%
Stop dalteparin. Start a direct oral anticoagulant for 3 months	69%
Stop dalteparin. Start a direct oral anticoagulant for 6 months	21%
Keep on dalteparin for 6 weeks	2%
Keep on dalteparin for 3 months	7%

As this patient developed a pulmonary embolism secondary to something (in this case severe illness with associated immobility) an anticoagulation period of 3 months is generally recommended.



Discuss (2)
Improve

[Next question >](#)

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)
 - interim therapeutic anticoagulation used to mean giving low-molecular weight heparin
 - NICE updated their guidance in 2020. They now recommend using an anticoagulant that can be continued if the result is positive.
 - this means normally a direct oral anticoagulant (DOAC) such as apixaban or rivaroxaban
- if the scan is negative but the D-dimer is positive:
 - stop interim therapeutic anticoagulation
 - offer a repeat proximal leg vein ultrasound scan 6 to 8 days later

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test
 - this should be done within 4 hours. If not, interim therapeutic anticoagulation should be given until the result is available
 - if the result is negative then DVT is unlikely and alternative diagnoses should be considered
 - if the result is positive then a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if a proximal leg vein ultrasound scan cannot be carried out within 4 hours interim therapeutic anticoagulation should be administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

D-dimer tests

- NICE recommend either a point-of-care (finger prick) or laboratory-based test
- age-adjusted cut-offs should be used for patients > 50 years old



Management

The cornerstone of VTE management is anticoagulant therapy. This was historically done with warfarin, often preceded by heparin until the INR was stable. However, the development of DOACs, and an evidence base supporting their efficacy, has changed modern management.

Choice of anticoagulant

- the big change in the 2020 guidelines was the increased use of DOACs
- apixaban or rivaroxaban (both DOACs) should be offered first-line following the diagnosis of a DVT
 - instead of using low-molecular weight heparin (LMWH) until the diagnosis is confirmed, NICE now advocate using a DOAC once a diagnosis is suspected, with this continued if the diagnosis is confirmed
 - if neither apixaban or rivaroxaban are suitable then either LMWH followed by dabigatran or edoxaban OR LMWH followed by a vitamin K antagonist (VKA, i.e. warfarin)
- if the patient has active cancer
 - previously LMWH was recommended
 - the new guidelines now recommend using a DOAC, unless this is contraindicated
- if renal impairment is severe (e.g. $\text{CrCl} < 15 \text{ ml/min}$) then LMWH, unfractionated heparin or LMWH followed by a VKA

- if the patient has antiphospholipid syndrome (specifically 'triple positive' in the guidance) then LMWH followed by a VKA should be used

Length of anticoagulation

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer at increased risk
 - an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



123



Next question >

B

I



A



T





Textbooks

High-yield textbook

Extended textbook

Links

NICE

 25  9

2020 Venous thromboembolism guidelines

[Suggest link](#)

[Report broken link](#)

Media



Deep vein thrombosis


Osmosis - YouTube

 3  0



Understanding Deep Vein Thrombosis (DVT)

Zero To Finals - YouTube

 2  1









Deep Vein Thrombosis - Overview (pathophysiology, treatment, complications)

Armando Hasudungan - YouTube

 3  2

[Report broken media](#)

Score: **13.9%**

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A 68-year-old gentleman with known chronic lymphocytic leukaemia (CLL) is reviewed in the Haematology Clinic.

He is normally an active gentleman who enjoys playing golf 3 times per week, but he complains that he has been feeling increasingly fatigued since his last appointment 6 months previously. He states that he has not been able to play golf for several weeks and his wife tells you that he has started napping during the afternoons. His past medical history is otherwise unremarkable and he takes no regular medications.

Examination reveals a tired gentleman with marked axillary and inguinal lymphadenopathy. His abdomen is soft with mild upper abdominal tenderness. A liver edge is palpable 3cm below the costal margin and his spleen is markedly enlarged.

His full blood count today is as follows:

Hb	114 g/l
Platelets	$173 \times 10^9/l$
WBC	$30.4 \times 10^9/l$
Neutrophils	$5.8 \times 10^9/l$
Lymphocytes	$23.1 \times 10^9/l$

His lymphocyte count 2 months ago was $15.3 \times 10^9/l$ and a decision to start the patient on fludarabine, cyclophosphamide, and rituximab (FCR) chemotherapy is taken.

Given the proposed treatment strategy, which of the following prophylactic medications is it most important to start?

- ☐ Co-trimoxazole ×
- ☐ Aciclovir ×
- ☐ Entecavir ×
- ☐ Fluconazole ×
- ☐ Penicillin V ×

Submit answer

Score: **12%**

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Lymphocytes	$23.1 \times 10^9/l$

His lymphocyte count 2 months ago was $15.3 \times 10^9/l$ and a decision to start the patient on fludarabine, cyclophosphamide, and rituximab (FCR) chemotherapy is taken.

Given the proposed treatment strategy, which of the following prophylactic medications is it most important to start?

Co-trimoxazole	58%
Aciclovir	13%
Entecavir	6%
Fluconazole	8%
Penicillin V	15%

Fludarabine is a purine analogue that prevents DNA synthesis through the inhibition of

ribonucleotide reductase and DNA polymerase. It is associated with profound lymphopenia, and significantly increases the risk of opportunistic infections. Patients treated with fludarabine are at particular risk of morbidity and mortality secondary to pneumocystis pneumonia. It is essential that these patients receive regular prophylactic co-trimoxazole.

Purine analogues can lead to herpes simplex, herpes zoster, and cytomegalovirus reactivation and aciclovir is often given as prophylaxis against this. Fluconazole is also frequently given as fungal prophylaxis.

Entecavir is given to patients who are hepatitis B surface antigen (HBsAg) positive.

Penicillin V is given to patients with asplenia and is not routinely used in this setting.

Pneumocystis pneumonia is the most severe complication described. Co-trimoxazole is, therefore, the most essential of the medications listed above.

		 Discuss (2)	Improve
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Next question >

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (> 10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy

Next question >



Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

 3  4

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)



Medicosis Perfectionalis - YouTube

 3  2



[Chronic leukemia](#)

Osmosis - YouTube

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[Report broken media](#)

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A 77-year-old lady was seen in the haematology outpatient clinic for her monthly follow-up. She has been seen in the haematology clinic for the last six months having been referred by her GP following an anomaly on her blood investigations. Overall she has been feeling well though for the last three weeks she has been feeling increasingly tired. She has noted that her appetite has been reduced for the last three months though she has not lost any weight during this time. In spite of the tiredness she is still able to lead an active life, regularly enjoying long distance rambling and gardening. She denied the presence of other symptoms, including the absence of fever or night sweats. She has a past medical history comprising asthma, hypertension, type 2 diabetes mellitus and hypercholesterolaemia for which she has been prescribed felodipine 5mg M/R OD, atorvastatin 20mg ON, Clenil modulite 2 puffs BD and metformin 500mg TDS.

Examination revealed the presence of a well elderly lady who was independently mobile. Her blood pressure was 122/82 mmHg, heart rate 82bpm and temperature 36.9 Celsius. Examination of her cardiovascular and respiratory systems revealed the presence of normal heart and breath sounds and a JVP of 3cm. Examination of her gastrointestinal and lymphatic systems revealed the presence of a smooth edge 2 fingerbreadths below the left subcostal margin and bilateral small cervical lymphadenopathy, with the maximum node size less than 1cm.

Investigations reveal the following:

Results from clinic three months ago:

Hb	112 g/l
Platelets	242 * 10 ⁹ /l
WBC	22.6 * 10 ⁹ /l
Neutrophils	2.1 * 10 ⁹ /l
Lymphocytes	19.9 * 10 ⁹ /l
Eosinophils	0.4 * 10 ⁹ /l
Monocytes	0.2 * 10 ⁹ /l

Renal and liver function tests were normal.

Blood film: lymphocytosis with atypical lymphocytes

Bone marrow aspirate: infiltration with 25% lymphocytes

Peripheral blood flow cytometry: presence of circulating clonal B-lymphocytes expressing CD5, CD19, CD20, CD 23, and an absence of FMC-7 staining

Results from clinic on this occasion:

Hb	106 g/l
----	---------

Platelets	162 * 10 ⁹ /l
WBC	34.2 * 10 ⁹ /l
Neutrophils	2.3 * 10 ⁹ /l
Lymphocytes	31.5 * 10 ⁹ /l
Eosinophils	0.3 * 10 ⁹ /l
Monocytes	0.1 * 10 ⁹ /l

What is the single next best step management step?

- ☐ Commence prednisolone therapy
- ☐ Commence chlorambucil therapy
- ☐ Commence fludarabine therapy
- ☐ Commence rituximab therapy
- ☐ Observe in clinic and repeat tests in one month

Submit answer

Reference ranges ▾

Score: 12%

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What is the single next best step management step?

Commence prednisolone therapy	3%
Commence chlorambucil therapy	13%
Commence fludarabine therapy	21%
Commence rituximab therapy	11%
Observe in clinic and repeat tests in one month	53%

This lady has chronic lymphocytic leukaemia (CLL) as manifested by the high lymphocyte count, lymphocyte marrow infiltration and evidence clinically of splenomegaly and lymphadenopathy. 70% of patients are asymptomatic and patients with stage A leukaemia as with this lady [no anaemia or thrombocytopaenia and less than 3 areas of lymphoid enlargement] have a median survival of 8 years. Treatment is therefore not indicated.

Accepted indications for treatment include:

- The development of anaemia +/- thrombocytopaenia
- Progressive or massive splenomegaly (6cm) +/- lymphadenopathy (10cm)
- Progressive lymphocytosis [50% increase in 2 months or doubling time of less than 6 months]
- Systemic symptoms [fever, night sweats, weight loss >10% in 6 months, extreme fatigue]

Although this lady has been complaining of tiredness, this does not in itself constitute a 'systemic symptom' given the absence of other symptoms and her strong performance status. Her lymphocyte count is rising but does not meet the criteria for treatment at present. Should treatment be indicated, this comprises chemotherapeutic agents such as chlorambucil and fludarabine, immunological agents such as rituximab and steroids in advanced disease.

		 Discuss (13)	Improve
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Next question >

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
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- massive (>6 cm) or progressive splenomegaly
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- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

[2012 CLL guidelines](#)

👍 3 🗨️ 4

Media



Chronic Lymphocytic Leukemia (CLL) - Diagnosis & Treatment

Medicosis Perfectionalis - YouTube

👍 3 👎 2



Chronic leukemia

Osmosis - YouTube

👍 2 👎 2

[Report broken media](#)

Score: **13.9%**

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A 32-year-old patient who is 10 weeks pregnant attends for her antenatal booking clinic. This is her first pregnancy, and she tells you she has been feeling lethargic and has a poor appetite. She has no past medical history of note.

On examination, she looks pale and appears comfortable at rest. Her chest is clear, heart sounds I&II are present and her abdomen is soft non-tender. She has some oedema of both ankles bilaterally. Her blood pressure is 111/75 mmHg and her heart rate is 79/min.

Investigations in clinics are as follows:

Hb	94 g/l
MCV	69 fl
Platelets	$168 \times 10^9/l$
WBC	$9.1 \times 10^9/l$
Hb electrophoresis	positive HbA2
Rhesus	negative
Blood Group	AB

Na ⁺	139 mmol/l
K ⁺	3.9 mmol/l
Urea	7.6 mmol/l
Creatinine	99 μ mol/l

What is the single most likely underlying condition?

<input type="radio"/> Alpha thalassaemia trait	×
<input type="radio"/> Beta thalassaemia trait	×
<input type="radio"/> Beta thalassemia major	×
<input type="radio"/> Iron deficiency anaemia	×
<input type="radio"/> Sideroblastic anaemia	×

Submit answer

Score: **12%**

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A 32-year-old patient who is 10 weeks pregnant attends for her antenatal booking clinic. This is her first pregnancy, and she tells you she has been feeling lethargic and has a poor appetite. She has no past medical history of note.

On examination, she looks pale and appears comfortable at rest. Her chest is clear, heart sounds I&II are present and her abdomen is soft non-tender. She has some oedema of both ankles bilaterally. Her blood pressure is 111/75 mmHg and her heart rate is 79/min.

Investigations in clinics are as follows:

Hb	94 g/l
MCV	69 fl
Platelets	$168 \times 10^9/l$
WBC	$9.1 \times 10^9/l$
Hb electrophoresis	positive HbA2
Rhesus	negative
Blood Group	AB

Na ⁺	139 mmol/l
K ⁺	3.9 mmol/l
Urea	7.6 mmol/l
Creatinine	99 μ mol/l

What is the single most likely underlying condition?

Alpha thalassaemia trait	13%
Beta thalassaemia trait	77%
Beta thalassemia major	6%
Iron deficiency anaemia	4%
Sideroblastic anaemia	1%

The two main differentials in this patient who has been identified as having a symptomatic

microcytic anaemia during pregnancy are iron deficiency anaemia and beta thalassaemia trait. The clue that this is beta thalassaemia trait rather than iron deficiency anaemia is that the MCV is surprisingly low for the level of haemoglobin. In iron deficiency anaemia you would expect the MCV to be much higher for a fairly modest decrease in haemoglobin.

In addition, the Hb electrophoresis shows +ve HbA2 which supports the diagnosis of beta thalassaemia trait. Of course, it would be wise to send off iron studies in this patient to assess for a coexistent iron deficiency anaemia.

Discuss (9)

Improve

Next question >

Beta-thalassaemia trait ★

The thalassaemias are a group of genetic disorders characterised by a reduced production rate of either alpha or beta chains. Beta-thalassaemia trait is an autosomal recessive condition characterised by a mild hypochromic, microcytic anaemia. It is usually asymptomatic

Features

- mild hypochromic, microcytic anaemia - microcytosis is characteristically disproportionate to the anaemia
- HbA2 raised (> 3.5%)

+

Q

123

Next question >

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Textbooks

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Links

Rare Disease Video Library - NORD

👍 6 👎 4

[Beta-thalassaemia](#)

Patient.info

👍 10 👎 5

[Thalassaemia review](#)

[Suggest link](#)

[Report broken link](#)

Media



[Beta-thalassaemia](#)

Osmosis - YouTube

👍 7 👎 0



[Thalassemia](#)

AK lectures - YouTube

👍 3 👎 0

[Report broken media](#)

Score: **13.9%**

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Question 96 of 191



A 54-year-old gentleman is reviewed 48 hours after being admitted to his local hospital with neutropaenic sepsis. He measured his temperature at home found it to be 38.2°C. Because of this, he called the chemotherapy helpline and he was advised to attend the emergency department who promptly admitted him under the care of the medical team.

He has a background of metastatic colorectal cancer and he has had chemotherapy ten days ago. He was started on piperacillin with tazobactam on admission. His temperature settled within 12 hours and investigations, including blood cultures, a chest X-ray, urine testing and a thorough examination did not find any source of infection. His initial neutrophil count was $0.4 \times 10^9/l$. Recent blood tests demonstrate a neutrophil count of $0.5 \times 10^9/l$. His vital parameters have all been normal since his temperature settled and he has not noticed any symptoms at any point.

What is the most appropriate management plan?

- ☐ Convert patient to oral antibiotics and discharge ×
- ☐ Keep on IV antibiotics in hospital until full course completed ×
- ☐ Monitor neutrophil count in hospital and discharge when greater than $1 \times 10^9/l$ ×
- ☐ Arrange for outpatient IV antibiotics ×
- ☐ Change piperacillin with tazobactam to meropenem ×

Submit answer

Reference ranges 

Score: 12%

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A 54-year-old gentleman is reviewed 48 hours after being admitted to his local hospital with neutropaenic sepsis. He measured his temperature at home found it to be 38.2°C. Because of this, he called the chemotherapy helpline and he was advised to attend the emergency department who promptly admitted him under the care of the medical team.

He has a background of metastatic colorectal cancer and he has had chemotherapy ten days ago. He was started on piperacillin with tazobactam on admission. His temperature settled within 12 hours and investigations, including blood cultures, a chest X-ray, urine testing and a thorough examination did not find any source of infection. His initial neutrophil count was $0.4 \times 10^9/\text{l}$. Recent blood tests demonstrate a neutrophil count of $0.5 \times 10^9/\text{l}$. His vital parameters have all been normal since his temperature settled and he has not noticed any symptoms at any point.

What is the most appropriate management plan?

Convert patient to oral antibiotics and discharge	22%
Keep on IV antibiotics in hospital until full course completed	27%
Monitor neutrophil count in hospital and discharge when greater than $1 \times 10^9/\text{l}$	40%
Arrange for outpatient IV antibiotics	4%
Change piperacillin with tazobactam to meropenem	6%

The correct answer is to convert patient to oral antibiotics and discharge. This is a patient who was admitted with a fever and a low neutrophil count and therefore he was managed with empirical IV antibiotics for neutropenic sepsis. Many of these patients will not look or feel significantly unwell and in the majority of them identifying a source of the temperature can be impossible. If neutropenic they should be treated with urgent IV antibiotics and waiting for a full blood count to confirm the low neutrophil count would be inappropriate. At 48 hours the antibiotic should be reviewed and if still febrile then escalation of antibiotics should be considered. If they have improved and the temperature has settled then there can be a consideration of an oral switch or if completely well can stop antibiotics altogether. NICE does not recommend keeping patients in hospital whilst waiting for their neutrophil count to improve.

Source:

'Neutropenic sepsis: prevention and management in people with cancer.' Clinical guideline



Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



123



Next question >

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Textbooks

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Links

Christies

👍 11 👎 7

[2013 Neutropenic sepsis guidelines](#)

NICE

👍 9 👎 3

[2012 Neutropenic sepsis guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Febrile Neutropenia](#)

Townsend Teaching - YouTube

👍 1 👎 0



What is febrile neutropaenia (neutropenia)? - neutrophil function, pathophysiology, treatment

Armando Hasudungan - YouTube

👍 2 👎 1



Neutropenic sepsis

Oncology for Medical Students - YouTube

👍 5 👎 3

[Report broken media](#)

Score: **13.9%**

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Question 97 of 191



A 67-year-old gentleman presents to the emergency department following a fall. He tripped on the carpet and landed on his back. Following this he has been complaining of lower back pain, but this pain was present prior to his fall and only slightly worsened with the accident. He undergoes a CT scan which unfortunately demonstrates lytic lesions in his lumbar vertebrae. He is suspected of having multiple myeloma. He undergoes blood and urine tests which unfortunately raises further suspicion of the diagnosis. He is due to undergo a bone marrow biopsy. What investigation prior to the biopsy can give prognostic information?

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| <input type="radio"/> | B2 microglobulin | × |
| <input type="radio"/> | Serum corrected calcium | × |
| <input type="radio"/> | Protein electrophoresis | × |
| <input type="radio"/> | Urine electrophoresis | × |

Submit answer

Reference ranges ▾

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A 67-year-old gentleman presents to the emergency department following a fall. He tripped on the carpet and landed on his back. Following this he has been complaining of lower back pain, but this pain was present prior to his fall and only slightly worsened with the accident. He undergoes a CT scan which unfortunately demonstrates lytic lesions in his lumbar vertebrae. He is suspected of having multiple myeloma. He undergoes blood and urine tests which unfortunately raises further suspicion of the diagnosis. He is due to undergo a bone marrow biopsy. What investigation prior to the biopsy can give prognostic information?

Serum immunofixation	3%
B2 microglobulin	72%
Serum corrected calcium	7%
Protein electrophoresis	13%
Urine electrophoresis	5%

The correct answer is B2 microglobulin. This is a patient who has unfortunately found to have multiple myeloma and is awaiting further investigation to obtain histology. B2 microglobulin elevation and fall in albumin are associated with a poor prognosis. Serum immunofixation and electrophoresis studies are useful diagnostic tools but are not as useful in terms of prognosis.

Source:

'Myeloma: diagnosis and management.' NICE guideline [NG35]. The National Institute for Health and Care Excellence, February 2016.



Discuss (2)
Improve

[Next question >](#)

Myeloma: prognosis ★

B2-microglobulin is a useful marker of prognosis - raised levels imply poor prognosis. Low levels of albumin are also associated with a poor prognosis

International prognostic index

Stage	Criteria	Median survival (months)
I	B2 microglobulin < 3.5 mg/l Albumin > 35 g/l	62
II	Not I or III	45
III	B2 microglobulin > 5.5 mg/l	29

Next question >

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Textbooks


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Links

British Committee for Standards in Haematology


2014 myeloma guidelines


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Cancer.net

Multiple Myeloma: Stages

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 1

Suggest link

Report broken link

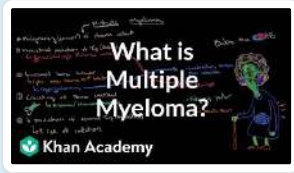
Media



Multiple Myeloma

Townsend Teaching - YouTube

👍 1 🗑️ 0



What is multiple myeloma?

Khan Academy - YouTube

👍 1 🗑️ 0



Multiple Myeloma

Medicosis Perfectionalis - YouTube

👍 1 🗑️ 0



Multiple Myeloma - Diagnosis and Treatment

Medicosis Perfectionalis - YouTube

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Multiple Myeloma Mnemonic...the story of the plasma cell

Medicosis Perfectionalis - YouTube

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Multiple Myeloma

CRASH! Medical Review - YouTube

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Multiple Myeloma

Armando Hasudungan - YouTube

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Question 98 of 191



A 45-year-old man undergoing chemotherapy mentions to the nurses that he has been feeling unwell for the last two days. He has currently having treatment for metastatic lung cancer. The nurses find that his temperature is 38.2°C. His other observations are stable. He has been having chemotherapy via a peripherally inserted central catheter (PICC). On examination his line site appears normal, his chest his clear and his abdomen is soft and non-tender. What is the most appropriate next step in his management plan?

- ☐ Send a full blood count to tests neutrophil levels ×
- ☐ Remove the PICC line and then observe if temperature settles ×
- ☐ Remove the PICC line then discharge with IV antibiotics ×
- ☐ Take blood cultures from the PICC line and peripherally then treat with IV antibiotics ×
- ☐ Discharge with oral antibiotics ×

Submit answer

Reference ranges 

Score: 12%

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Question 98 of 191



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Send a full blood count to tests neutrophil levels

16%

Remove the PICC line and then observe if temperature settles

1%

Remove the PICC line then discharge with IV antibiotics

2%

Take blood cultures from the PICC line and peripherally then treat with IV antibiotics

80%

Discharge with oral antibiotics

1%

The correct answer is to take blood cultures from the PICC line and peripherally then treat with IV antibiotics. This is a patient on chemotherapy who has developed an asymptomatic fever at 38.2°C. As he may be neutropenic, he should be admitted to hospital and given IV piperacillin and tazobactam, but blood cultures should be taken from any central lines that he has before doing so. If a line has more than one port then blood cultures should be taken from each port. Peripherally inserted lines should only be removed if they are shown to be the cause of infection, which is why blood cultures from these lines are important.

Source:

'Neutropenic sepsis: prevention and management in people with cancer.' NICE guideline [CG151]. The National Institute for Health and Care Excellence, September 2012.



Discuss (3)

Improve

Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



123



Next question >

B

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A



T





Textbooks

High-yield textbook

Extended textbook



Links

Christies

 11  7

[2013 Neutropenic sepsis guidelines](#)

NICE

 9  3

[2012 Neutropenic sepsis guidelines](#)

[Suggest link](#)



[Report broken link](#)

Media



[Febrile Neutropenia](#)



Townsend Teaching - YouTube

 1  0



[What is febrile neutropaenia \(neutropenia\)? - neutrophil function, pathophysiology, treatment](#)

Armando Hasudungan - YouTube

 2  1



[Neutropenic sepsis](#)

Oncology for Medical Students - YouTube

 5  3

[Report broken media](#)

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A 50-year-old man is diagnosed with high-grade non-Hodgkin's lymphoma and starts his regimen of R-CHOP chemotherapy. Two days after his chemotherapy he complains of feeling increasingly weak, lethargic and generally unwell. He has developed persistent vomiting and is unable to tolerate oral fluids.

He has a history of recurrent gout but has been unable to tolerate allopurinol.

On examination, he looks unwell and pale. He seemed short of breath with a respiratory rate of 28 per minute. His temperature is 36.5°C, heart rate 110 bpm, blood pressure 100/60 mmHg.

His heart sounds were normal. His JVP was raised by 4cm lying at 45 degrees in the bed. Examination of the chest revealed fine bibasal inspiratory crepitations. Pitting oedema was present to mid-shins bilaterally.

Abdominal examination was unremarkable.

On neurological examination, there was normal tone and sensation to all limbs. General weakness was noted.

The house officer has taken bloods:

Na+	137 mmol/L
K+	6.2 mmol/L
Urea	15 mmol/L (previously 8)
Creatinine	240 µmol/L (previously 100)
Hb	100 g/L
WBC	$10.0 \times 10^9/L$
Corrected Calcium	1.95 mmol/L
Phosphate	2.3 mmol/L
Uric acid	640 mmol/L
LFTs	Normal

Chest x-ray shows congested lung fields.

ECG demonstrates tall T waves.

In view of the diagnosis which of the following is most likely to treat the hyperuricaemia?

<input type="radio"/>	IV calcium gluconate, insulin and dextrose infusion	×
<input type="radio"/>	Allopurinol	×
<input type="radio"/>	Rasburicase	×
<input type="radio"/>	IV fluids	×
<input type="radio"/>	IV electrolyte replacement	×

Submit answer

Reference ranges ▾

Score: **12%**

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Phosphate	2.3 mmol/L
Uric acid	640 mmol/L
LFTs	Normal

Chest x-ray shows congested lung fields.


ECG demonstrates tall T waves.

In view of the diagnosis which of the following is most likely to treat the hyperuricaemia?

IV calcium gluconate, insulin and dextrose infusion	7%
Allopurinol	3%
Rasburicase	79%
IV fluids	10%
IV electrolyte replacement	1%

This man has lymphoma and has presented with physical and biochemical markers suggesting established tumour lysis syndrome. He has severe electrolyte disturbance: hyperkalaemia, hypocalcaemia, hyperphosphataemia. The chest x-ray suggests pulmonary oedema and ECG indicates a degree of cardiac toxicity from the hyperkalaemia. There is also acute renal failure and hyperuricaemia.

The question asks what treatment should be used to treat the underlying condition of tumour lysis syndrome. The answer is rasburicase as he has previously been intolerant of allopurinol in the context of gout prophylaxis. All the other answers are entirely reasonable and are part of the treatment of tumour lysis syndrome but do not answer this question specifically.



Discuss (4)
Improve

Next question >

Tumour lysis syndrome ★

Tumour lysis syndrome (TLS) is a potentially deadly condition related to the treatment of high-grade lymphomas and leukaemias. It can occur in the absence of chemotherapy but is usually triggered by the introduction of combination chemotherapy. On occasion, it can occur with steroid treatment alone. Awareness of the condition is critical as prophylactic medication can be given to prevent the potentially deadly effects of tumour cell lysis.

TLS occurs from the breakdown of the tumour cells and the subsequent release of chemicals from the cell. It leads to a high potassium and high phosphate level in the presence of a low calcium. It should be suspected in any patient presenting with an acute kidney injury in the presence of a high phosphate and high uric acid level.

Prevention

- IV fluids
- patients at higher risk should receive either allopurinol or rasburicase
- rasburicase

- a recombinant version of urate oxidase, an enzyme that metabolizes uric acid to allantoin. Allantoin is much more water-soluble than uric acid and is, therefore, more easily excreted by the kidneys
- generally preferred now for patients at a higher risk of developing TLS
- allopurinol
 - generally used for patients in lower-risk groups
- rasburicase and allopurinol should not be given together in the management of tumour lysis syndrome as this reduces the effect of rasburicase

From 2004 TLS has been graded using the Cairo-Bishop scoring system -

Laboratory tumor lysis syndrome: abnormality in two or more of the following, occurring within three days before or seven days after chemotherapy.

- uric acid > 475umol/l or 25% increase
- potassium > 6 mmol/l or 25% increase
- phosphate > 1.125mmol/l or 25% increase
- calcium < 1.75mmol/l or 25% decrease

Clinical tumor lysis syndrome: laboratory tumour lysis syndrome plus one or more of the following:

- increased serum creatinine (1.5 times upper limit of normal)
- cardiac arrhythmia or sudden death
- seizure



123



Next question >

B

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A



Textbooks



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Media





Tumour Lysis Syndrome

Oncology for Medical Students - YouTube  2  0





Tumour Lysis Syndrome in 3 Minutes

Townsend Teaching - YouTube  1  0



Tumour lysis syndrom

Armando Hasudungan - YouTube  5  1

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Score: **13.9%**

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Question 100 of 191



An 85-year-old male is referred by the anaesthetic registrar after abnormal blood test results were noted during pre-assessment for an elective hip replacement. He is otherwise fit and well, independent with all activities of daily living and continues to drive. His past medical history includes diet controlled type 2 diabetes mellitus and hypertension. On examination, he is alert and well, reports no discomfort, pain, or non-specific malaise. No skin bruises or conjunctival pallor are noted. You note a rubbery, non-tender and firm 3cm lymph node in the left cervical chain and non-tender splenomegaly at 8cm below the costal margin. His chest is clear and normal heart sounds are noted. His blood tests are as follows, with blood tests from his GP 6 months ago in brackets:

Hb	89 (95) g/l
Platelets	78 (76) * $10^9/l$
WBC	67 (32) * $10^9/l$
Blood film	mature lymphocytes and smudge cells

What is the most appropriate treatment?

- ☐ Monitor and repeat blood count in 6 months ×
- ☐ Fludarabine, cyclophosphamide and rituximab treatment immediately ×
- ☐ Delayed chlorambucil treatment in 6 months ×
- ☐ Platelet transfusion ×
- ☐ Intravenous immunoglobulin ×

Submit answer

Reference ranges 

Score: 12%

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Hb	89 (95) g/l
Platelets	78 (76) * 10 ⁹ /l
WBC	67 (32) * 10 ⁹ /l
Blood film	mature lymphocytes and smudge cells

What is the most appropriate treatment?





Monitor and repeat blood count in 6 months	29%
Fludarabine, cyclophosphamide and rituximab treatment immediately	67%
Delayed chlorambucil treatment in 6 months	2%
Platelet transfusion	0%
Intravenous immunoglobulin	1%

This patient is on the cusp of requiring immediate treatment for chronic lymphocytic leukaemia. The latest guidelines are provided by the British Committee for Standards in Haematology (BCSH) 2012¹, recommending immediate treatment to commence if the patient demonstrates signs of progressive marrow failure, massive or symptomatic splenomegaly greater than 6cm below the costal margin, massive or symptomatic nodes greater than 10cm in longest diameter, progressive lymphocytosis with doubling in 6 months, autoimmune thrombocytopaenia or anaemia, or significant constitutional symptoms within the previous 6 months. It is important to note that doubling of lymphocytosis is calculated only if the initial count is greater than 30 x 10⁹/l.

Asymptomatic patients not meeting these criteria do not benefit in long term survival when receiving immediate chlorambucil therapy versus delayed treatment². Regular blood test monitoring is more appropriate for this group of patients. Be aware that despite increased white

cell counts, the mature lymphocytes are non-functional and patients are hence at increased risk of infections. Intravenous immunoglobulin may be appropriate if the patient shows features of a significant infection. Similarly, significant progressive marrow failure, demonstrated by symptomatic anaemia or thrombocytopaenia may require replacement. In this case, the patient fits criteria for immediate treatment based on his lymphocytosis doubling time and splenomegaly.

1. British Committee for Standards in Haematology (BCSH) 2012
2. Chemotherapeutic options in chronic lymphocytic leukaemia: a meta-analysis of the randomised trials. CLL Trialists' Collaborative Group. J Natl Cancer Inst. 1999;91(10):861

   Discuss (10)  Improve

Next question >

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (> 10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

Management


- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy

 + Q 123 


Next question >


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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

 3  4

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)



Medicosis Perfectionalis - YouTube

 3  2




[Chronic leukemia](#)


Osmosis - YouTube


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A 77-year-old female is referred to the hospitals ambulatory care clinic by her GP after 2 months of increasing generalised malaise and 'lack of energy' over the past two months. She lives with her husband and until 9 weeks ago, continued to drive and go for walks in the countryside with no limitations to her exercise tolerance. Now, she feels 'tired all the time' but denies any problems with her mood. She has no history of psychiatric disorders. Her past medical history includes hypertension (well controlled on ramipril alone), hypercholesterolaemia (well controlled on simvastatin) and chronic lymphocytic leukaemia, diagnosed 3 years ago and not requiring treatment.

On examination, she has warm peripheries with bilateral conjunctival pallor. She is alert and comfortable at rest. Non-tender lymphadenopathy in bilateral cervical chains. Her cardiovascular, respiratory, abdominal and neurological examinations are otherwise unremarkable. Her blood results are as follows:

Hb	72 g/l
MCV	101 fl
Platelets	$70 \times 10^9/l$
WBC	$67.0 \times 10^9/l$
Neut	$4.0 \times 10^9/l$
WBC	$62.0 \times 10^9/l$
Reticulocytes	14%
Blood film and direct agglutination test	lymphocytosis, smudge cells, reticulocytes, red cell agglutination at physiological temperature


What is the most likely cause of this patient's anaemia?

Cold autoimmune haemolytic anaemia	14%
Warm autoimmune haemolytic anaemia	75%
B12 deficiency anaemia	4%
Iron deficiency anaemia	1%
Microangiopathic haemolytic anaemia	6%

The patient presents with a borderline macrocytic/normocytic anaemia with a positive Coombs test at 37 degree temperature, suggesting an autoimmune haemolytic anaemia. The presence of

red cell agglutination at a warm temperature suggests the presence of IgG on red blood cells, which in vivo leads to phagocytosis by a granulocyte: this is warm autoimmune haemolytic anaemia. Conversely, red cell agglutination at cold temperatures, typically between 0 and 4 degrees, suggests the presence of IgM and C3 component of complement, most commonly leading to direct cell lysis by the complement system: this is cold autoimmune haemolytic anaemia. A mildly raised or borderline MCV does not necessarily guarantee a macrocytic cause in this context: the high proportion of reticulocytes in the blood demonstrates increased red cell production from marrow, increasing the release of immature cells with higher corpuscular volume than mature red cells, hence the increased MCV in blood assays. Iron deficiency anaemias typically produce microcytic anaemias with target cells. Microangiopathic haemolytic anaemia (MAHA) is caused by the mechanical destruction of red cells in conditions such as thrombotic thrombocytopenic purpura, leading to fragmented red cells (schistocytes) and a typically normocytic picture with associated thrombocytopenia.

Both warm and cold autoimmune haemolytic anaemias can be idiopathic or caused by lymphoproliferative disorders. Warm agglutinins are also more commonly produced by systemic autoimmune conditions such as SLE, rheumatoid arthritis and systemic sclerosis, while cold agglutinins are also classically triggered by mycoplasma and viral infections such as infectious mononucleosis.

		 Discuss (7)	Improve
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Next question >

Autoimmune haemolytic anaemia ★

Autoimmune haemolytic anaemia (AIHA) may be divided into 'warm' and 'cold' types, according to at what temperature the antibodies best cause haemolysis. It is most commonly idiopathic but may be secondary to a lymphoproliferative disorder, infection or drugs.

Investigations

- general features of haemolytic anaemia
 - anaemia
 - reticulocytosis
 - low haptoglobin
 - raised lactate dehydrogenase (LDH) and indirect bilirubin
 - blood film: spherocytes and reticulocytes
- specific features of autoimmune haemolytic anaemia
 - positive direct antiglobulin test (Coombs' test).

Warm AIHA

Warm is the most common type of AIHA. In warm AIHA the antibody (usually IgG) causes

haemolysis best at body temperature and haemolysis tends to occur in extravascular sites, for example the spleen.

Causes of warm AIHA

- idiopathic
- autoimmune disease: e.g. systemic lupus erythematosus*
- neoplasia
 - lymphoma
 - chronic lymphocytic leukaemia
- drugs: e.g. methyldopa

Management

- treatment of any underlying disorder
- steroids (+/- rituximab) are generally used first-line

Cold AIHA

The antibody in cold AIHA is usually IgM and causes haemolysis best at 4 deg C. Haemolysis is mediated by complement and is more commonly intravascular. Features may include symptoms of Raynaud's and acrocynaosis. Patients respond less well to steroids

Causes of cold AIHA

- neoplasia: e.g. lymphoma
- infections: e.g. mycoplasma, EBV

*systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia



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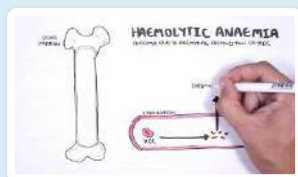
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Textbooks

High-yield textbook

Media



Haemolytic Anaemia - classification (intravascular, extravascular), pathophysiology, investigations

Armando Hasudungan - YouTube

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Warm autoimmune hemolytic anemia and cold agglutinin

Osmosis - YouTube

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Autoimmune haemolytic anaemia

Osmosis - YouTube

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Score: **13.9%**

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Question 102 of 191



A 57-year-old female presents to pre-assessment surgical clinic prior to an elective arthroscopy of her left knee that she injured while playing tennis. She is otherwise asymptomatic, has no other medical history and is a lifelong non-smoker. She drinks 10 units of alcohol per week. Recently, she has experienced hot flushes and irregular periods, which she puts down to undergoing the menopause. Examination of her cardiovascular, respiratory and abdominal systems are unremarkable.

Her blood results are as follows:

Hb	95 g/l
MCV	59 fl
Platelets	$389 \times 10^9/l$
WBC	$4.5 \times 10^9/l$
Red cell distribution width	13% (normal range 11.5-14.5%)
Blood film	anisocytosis, hypochromia, target cells

Which investigation is most likely to reveal the diagnosis?

- ☐ Serum ferritin ×
- ☐ Total iron binding capacity ×
- ☐ Serum iron ×
- ☐ Haemoglobin electrophoresis ×
- ☐ Bone marrow biopsy ×

Submit answer

Reference ranges 

Score: **13.9%**

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A 57-year-old female presents to pre-assessment surgical clinic prior to an elective arthroscopy of her left knee that she injured while playing tennis. She is otherwise asymptomatic, has no other medical history and is a lifelong non-smoker. She drinks 10 units of alcohol per week. Recently, she has experienced hot flushes and irregular periods, which she puts down to undergoing the menopause. Examination of her cardiovascular, respiratory and abdominal systems are unremarkable.

Her blood results are as follows:

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WBC	$4.5 \times 10^9/l$
Red cell distribution width	13% (normal range 11.5-14.5%)
Blood film	anisocytosis, hypochromia, target cells

Which investigation is most likely to reveal the diagnosis?

Serum ferritin	18%
Total iron binding capacity	9%
Serum iron	5%
Haemoglobin electrophoresis	63%
Bone marrow biopsy	5%

The patient is asymptomatic with a microcytic anaemia. Note the disproportionately lower MCV compared to the level of haemoglobin and the normal red cell distribution width: the first is a distinctive feature of thalassaemia beta minor (trait) while the second suggests that all red cells made by the marrow of similar haemoglobin quality, such as in an underlying genetic trait such as thalassaemia beta minor. In contrast, iron deficiency normally demonstrates a significant haemoglobin drop by the time MCV is at such a low value while increasing the RDW during early to mid stages of iron deficiency, as some red cells are produced normally while some are profoundly microcytic.

Diagnosis of thalassaemia beta minor is by haemoglobin electrophoresis. However, diagnosis of

iron deficiency is reliant on a combination of indicators: serum iron alone is not necessarily diagnostic as it also appears in anaemia of chronic disease. Serum ferritin is perhaps the most reliable indicator of plasma and marrow iron stores but be wary that it may be increased in inflammatory states, hence mask an underlying iron deficiency anaemia. Total iron binding capacity (TIBC) is a measure of transferrin, to which iron is bound to in plasma. Again, it is a useful indicator of iron stores but can be altered by pregnancy or the oral contraceptive pill. An iron deficiency anaemia picture is generally diagnosed by a combination of all three: low serum iron, high TIBC, low ferritin.

Discuss (3)

Improve

Next question >

Beta-thalassaemia trait ★

The thalassaemias are a group of genetic disorders characterised by a reduced production rate of either alpha or beta chains. Beta-thalassaemia trait is an autosomal recessive condition characterised by a mild hypochromic, microcytic anaemia. It is usually asymptomatic

Features

- mild hypochromic, microcytic anaemia - microcytosis is characteristically disproportionate to the anaemia
- HbA2 raised (> 3.5%)

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123

Next question >

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Score: **13.7%**

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- 102** ✗



A 57-year-old presents with recurrent episodes of bleeding gums, nosebleeds and intermittent haematuria over the past 6 weeks. He works as an accountant, does not have any past medical history but is an active smoker of 20 pack years. He drinks occasional alcohol.

On examination, scabs and dried blood are noted on mucous membranes. No arthritis or cutaneous abnormalities are noted. The nasal bridge is unremarkable. His conjunctiva appeared pale, respiratory, abdominal and cardiovascular examination was unremarkable. His blood tests are as follows:

Hb	37 g/l
MCV	87 fl
Platelets	$17 \times 10^9/l$
WBC	$44.0 \times 10^9/l$
Blood film	myeloblasts with elongated, needle-like cytoplasmic inclusions

Na ⁺	147 mmol/l
K ⁺	3.2 mmol/l
Urea	7.8 mmol/l
Creatinine	70 μ mol/l

What is the most likely underlying diagnosis?

- ☐ Acute myeloid leukaemia ×
- ☐ Acute lymphocytic leukaemia ×
- ☐ Chronic myeloid leukaemia ×
- ☐ Chronic lymphoid leukaemia ×
- ☐ Myelofibrosis ×

Submit answer

Reference ranges ∨

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Na^+	147 mmol/l
K^+	3.2 mmol/l
Urea	7.8 mmol/l
Creatinine	70 μ mol/l

What is the most likely underlying diagnosis?

Acute myeloid leukaemia	76%
Acute lymphocytic leukaemia	3%
Chronic myeloid leukaemia	10%
Chronic lymphoid leukaemia	3%
Myelofibrosis	9%

The diagnosis is made on blood film description of needle-like elongated cytoplasmic inclusions, known as Auer rods that are pathognomonic of acute myeloid leukaemia, with myeloblasts typical of myeloid leukaemias. Clinical features are frequently typical of cell line abnormalities secondary to marrow infiltration (shortness of breath on exertion, pallor caused by anaemia; bruising or bleeding caused by thrombocytopaenia) and infections secondary to dysfunctional white cells.

Diagnosis is confirmed by bone marrow biopsy, with blast cells accounting for greater than 20% of marrow cellularity. Immunophenotyping, cytogenetic and morphological analysis guides subsequent treatment options.



Discuss (3)

Improve

Next question >

Acute myeloid leukaemia ★

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Features are largely related to bone marrow failure:

- anaemia: pallor, lethargy, weakness
- neutropenia: whilst white cell counts may be very high, functioning neutrophil levels may be low leading to frequent infections etc
- thrombocytopenia: bleeding
- splenomegaly
- bone pain

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- Auer rods (seen with myeloperoxidase stain)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)

- M0 - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia

- M7 - megakaryoblastic



123



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Question 2 of 89



A 60-year-old female with known chronic lymphocytic leukaemia (CLL) presents with coryzal symptoms. Examination findings are unremarkable. Her blood tests are as follows:

	8 months previously	Two months previously	Today
Haemoglobin	113 g/l	108 g/l	106 g/l
White cell count	32.0 *10 ⁹ /l	50.0 *10 ⁹ /l	58.0 *10 ⁹ /l
Neutrophils	7.0 *10 ⁹ /l	4.8 *10 ⁹ /l	4.0 *10 ⁹ /l
Lymphocytes	25.0 *10 ⁹ /l	45.0 *10 ⁹ /l	54.0 *10 ⁹ /l
Platelets	358 *10 ⁹ /l	280 *10 ⁹ /l	268 *10 ⁹ /l

What is the most appropriate treatment option?

- ☐ Chlorambucil ×
- ☐ Fludarabine and chlorambucil ×
- ☐ Observation ×
- ☐ Prednisolone ×
- ☐ Fludarabine ×

Submit answer

Reference ranges 

Score: **0%**

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Question 2 of 89



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	8 months previously	Two months previously	Today
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Lymphocytes	25.0 *10 ⁹ /l	45.0 *10 ⁹ /l	54.0 *10 ⁹ /l
Platelets	358 *10 ⁹ /l	280 *10 ⁹ /l	268 *10 ⁹ /l

What is the most appropriate treatment option?

Chlorambucil	5%
Fludarabine and chlorambucil	33%
Observation	56%
Prednisolone	1%
Fludarabine	5%

CLL is typically an indolent disease which is often managed conservatively in the first instance. Indications for treatment are multiple but include constitutional symptoms, bone marrow failure and massive lymphadenopathy. Additionally, a lymphocyte doubling time of less than 6 months is an indication for treatment, but this is not met here. Chlorambucil, fludarabine and high dose corticosteroids are all possible therapeutic options in CLL.



 Discuss (6)
  Improve

Next question >

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (> 10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy



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British Committee for Standards in Haematology

[2012 CLL guidelines](#)



3



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Question 3 of 89



A 21-year-old male is admitted to hospital after his GP identified a pancytopenia following a workup for recent fatigue and weight loss. An hour after arrival he develops a sustained nosebleed. On review, you notice oozing from his cannula sites and non-blanching purpura over his arms and legs.

What is the most likely cause of this patient's presentation?

- ☐ Henoch-Schonlein purpura ×
- ☐ Aplastic anaemia ×
- ☐ Acute promyelocytic leukaemia ×
- ☐ Meningococcal septicaemia ×
- ☐ Idiopathic thrombocytopenic purpura ×

Submit answer

Reference ranges 

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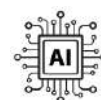
A 21-year-old male is admitted to hospital after his GP identified a pancytopenia following a workup for recent fatigue and weight loss. An hour after arrival he develops a sustained nosebleed. On review, you notice oozing from his cannula sites and non-blanching purpura over his arms and legs.

What is the most likely cause of this patient's presentation?

Henoch-Schonlein purpura	6%
Aplastic anaemia	21%
Acute promyelocytic leukaemia	60%
Meningococcal septicaemia	2%
Idiopathic thrombocytopenic purpura	10%

DIC is a severe complication of acute promyelocytic leukaemia

Important for me Less important



This patient has developed disseminated intravascular coagulopathy (DIC) secondary to acute promyelocytic leukaemia (APML). This is a potentially life-threatening complication of APML that is important to be aware of in patients presenting with features of leukaemia.

Henoch-Schonlein purpura does not result in a pancytopenia or bleeding. The purpuric rash present is typically on the lower limbs and secondary to a vasculitic process. Aplastic anaemia also presents with a pancytopenia, but the features suggestive of DIC in this patient point against this as the underlying diagnosis. Meningococcal septicaemia is an important differential to consider though would not be expected to result in complete marrow suppression. Finally, idiopathic thrombocytopenic purpura causes an isolated platelet drop.



Discuss (5)
Improve

Next question >

Acute myeloid leukaemia ★

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Features are largely related to bone marrow failure:

- anaemia: pallor, lethargy, weakness
- neutropenia: whilst white cell counts may be very high, functioning neutrophil levels may be low leading to frequent infections etc
- thrombocytopenia: bleeding
- splenomegaly
- bone pain

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

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- DIC or thrombocytopenia often at presentation
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- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic



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A 25 year old man is admitted to the acute medical unit and is treated for a left lobar pneumonia. Looking through his past medical history you note he has had 3 previous admissions with similar presentations in the last 5 years. He has no other past medical history of note, apart from what he describes as 'a few' episodes of sinusitis. His blood differential, after treatment of his pneumonia, is normal. His HIV test is also negative. What is the possible underlying diagnosis?

- ☐ Cystic fibrosis

×
- ☐ Selective IgA deficiency

×
- ☐ Wiskott-Aldrich syndrome

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- ☐ Acute lymphoblastic leukemia

×
- ☐ Digeorges syndrome

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Submit answer

Reference ranges ▾

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Question 4 of 89



A 25 year old man is admitted to the acute medical unit and is treated for a left lobar pneumonia. Looking through his past medical history you note he has had 3 previous admissions with similar presentations in the last 5 years. He has no other past medical history of note, apart from what he describes as 'a few' episodes of sinusitis. His blood differential, after treatment of his pneumonia, is normal. His HIV test is also negative. What is the possible underlying diagnosis?

Cystic fibrosis	9%
Selective IgA deficiency	69%
Wiskott-Aldrich syndrome	17%
Acute lymphoblastic leukemia	1%
Digeorges syndrome	4%

Selective immunoglobulin A deficiency:

- The most common primary antibody deficiency
- Affected patients may develop recurrent chest infections, bronchitis, sinusitis or even otitis media.
- Associated with atopic disorders such as asthma and atopic dermatitis.
- Some patients may also be at risk of severe transfusion reactions.

Wiskott-Aldrich syndrome:

- Characterised by a triad of recurrent chest infections/recurrent sinus infections
- Atopic dermatitis
- Thrombocytopenia and platelet dysfunction
- Inherited as an X linked recessive condition.



Discuss (2)
Improve

Next question >

Primary immunodeficiency ★

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
Chronic granulomatous disease	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. <i>Staphylococcus aureus</i> and fungi (e.g. <i>Aspergillus</i>) Negative nitroblue-tetrazolium test Abnormal dihydrorhodamine flow cytometry test
Chediak-Higashi syndrome	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen Giant granules in neutrophils and platelets
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen Absence of neutrophils/pus at sites of infection

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Low antibody levels, specifically in immunoglobulin (Ig) types IgG, IgM and IgA. Recurrent chest infections. May also predispose to autoimmune disorders and lymphoma
Bruton's (x-linked) congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen Absence of B-cells with reduced immunoglobulins of all classes
Selective immunoglobulin A deficiency	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and

Disorder	Underlying defect	Notes
		<p>respiratory infections</p> <p>Associated with coeliac disease and may cause false negative coeliac antibody screen</p> <p>Severe reactions to blood transfusions may occur (anti-IgA antibodies → anaphylaxis)</p>

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4th pharyngeal pouches	Common features include congenital heart disease (e.g. tetralogy of Fallot), learning difficulties, hypocalcaemia, recurrent viral/fungal diseases, cleft palate

Combined B- and T-cell disorders

Disorder	Underlying defect	Notes
Severe combined immunodeficiency	Many varying causes. Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. Other causes include adenosine deaminase deficiency	<p>Recurrent infections due to viruses, bacteria and fungi.</p> <p>Reduced T-cell receptor excision circles</p> <p>Stem cell transplantation may be successful</p>
Ataxic telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia (spider angiomas), recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	<p>X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopenia.</p> <p>Low IgM levels</p>

Disorder	Underlying defect	Notes
		Increased risk of autoimmune disorders and malignancy
Hyper IgM Syndromes	Mutations in the CD40 gene	Infection/ <i>Pneumocystis</i> pneumonia, hepatitis, diarrhoea

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[X linked agammaglobulinemia \(Bruton agammaglobulinemia\)](#)

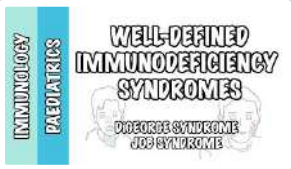
Osmosis - YouTube



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[Well defined genetic immunodeficiency - DiGeorge Syndrome and Job Syndrome](#)

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Leukocyte adhesion deficiency

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Selective immunoglobulin A deficiency

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👍 2 👎 1



Primary antibody deficiency - Common Variable Immunodeficiency (CVID) , X-linked agammaglobulinemia

Armando Hasudungan - YouTube

👍 2 👎 2



Digeorge syndrome (22q11.2 deletion syndrome)

Osmosis - YouTube

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A 57-year-old man presents to his General Practitioner with persistent headaches and blurred vision. The symptoms have been present over the past six months but have worsened in recent weeks. On close questioning, the patient also reported a feeling of general fatigue and intermittent muscle aches.

One year previously, the patient had been diagnosed with obstructive sleep apnoea secondary to morbid obesity and had been provided with non-invasive ventilation to use at night. However, the patient admitted that he rarely used this equipment due to a dislike for the tight face mask. Despite dietary and lifestyle advice the patient had gained 6 kg over the past year and had a BMI of 41 kg / m².

Neurological examination including fundoscopy was unremarkable. There were no tender or inflamed joints. Blood tests requested by the GP are detailed below.

Haemoglobin	195 g/L
White cell count	7.5 * 10 ⁹ /l
Neutrophils	5.7 * 10 ⁹ /l
Lymphocytes	0.9 * 10 ⁹ /l
Platelets	195 * 10 ⁹ /l
Packed cell volume	0.60
Urea	5.9 mmol / L
Creatinine	110 µmol / L
Sodium	135 mmol / L
Potassium	4.1 mmol / L
eGFR	68 ml / min

Review of a full blood count performed 4 months previously was remarkable for previously unnoticed elevated PCV of 0.56. The patient was urgently referred to haematology for further management.

What is the most appropriate treatment for this patient's erythrocytosis?

- ☐ Aspirin ×
- ☐ Venesection ×
- ☐ Hydroxyurea ×

☐ Improved compliance with nocturnal non-invasive ventilation ×

☐ Referral to weight management service ×

Submit answer

Reference ranges ▼

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eGFR	68 ml / min

Review of a full blood count performed 4 months previously was remarkable for previously unnoticed elevated PCV of 0.56. The patient was urgently referred to haematology for further management.

What is the most appropriate treatment for this patient's erythrocytosis?

Aspirin	3%
Venesection	54%
Hydroxyurea	12%

This patient has a secondary erythrocytosis secondary to hypoxia associated with his obstructive sleep apnoea. He is presenting with significant symptoms of hyperviscosity and should be considered to be at significant risk of thrombotic complications.

Evidence from small case series suggests that erythrocytosis secondary to OSA should be treated with venesection in the presence of hyperviscosity symptoms or a PCV > 0.56. A target PCV of 0.50-0.52 has been shown to increase exercise tolerance.

Aspirin is the mainstay of treatment in polycythaemia vera and cytoreductive treatments such as hydroxyurea are used in high-risk cases.

While weight-loss and improved compliance with OSA treatment may improve erythrocytosis these interventions are likely to require significant time prior to yielding any symptomatic benefit.

Keohane C, McMullin M, Harrison C. The diagnosis and management of erythrocytosis. BMJ 2013;347:f6667.



Discuss (8)

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Next question >

Polycythaemia ★

Polycythaemia may be relative, primary (polycythaemia rubra vera) or secondary

Relative causes

- dehydration
- stress: Gaisbock syndrome

Primary

- polycythaemia rubra vera

Secondary causes

- COPD
- altitude
- obstructive sleep apnoea

- excessive erythropoietin: cerebellar haemangioma, hypernephroma, hepatoma, uterine fibroids*

To differentiate between true (primary or secondary) polycythaemia and relative polycythaemia red cell mass studies are sometimes used. In true polycythaemia the total red cell mass in males > 35 ml/kg and in women > 32 ml/kg

*uterine fibroids may cause menorrhagia which in turn leads to blood loss - polycythaemia is rarely a clinical problem



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Links

British Committee for Standards in Haematology

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[2005 polycythaemia guidelines](#)

[Suggest link](#)

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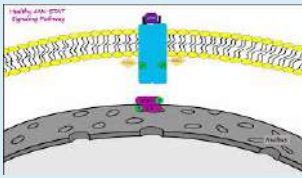
Media



[Polycythemia: Clinical Features, Management and Mnemonics](#)

Townsend Teaching - YouTube

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Polycythemia - part 1

PhysioPathoPharmaco - YouTube

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Polycythemia - part 2

PhysioPathoPharmaco - YouTube

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Question 6 of 89



You are working in haematology. A 72-year-old man has been referred to you by the general surgeons. He recently had a CT scan for weight loss and a two month change in bowel habit. This showed no lesions within the bowel but did demonstrate some mesenteric lymphadenopathy. The largest lymph node was 4 cm in diameter. He is otherwise well and has a background of hypertension and diet controlled diabetes. He subsequently underwent a CT guided biopsy (histology report below).

The lymph node biopsied lacks a mantle zone and is made up of a predominant population of centrocytes with few tangible body macrophages. Immunohistochemistry confirms strong positivity for CD20 as well as CD70a, CD10, BCL2 and BCL6. The proliferation index (Ki-67) is low, no more than 20%.

What is the most likely diagnosis?

- ☐ Nodular sclerosing lymphoma ×
- ☐ Lymphoplasmacytic lymphoma ×
- ☐ Follicular lymphoma ×
- ☐ Adenocarcinoma of the large bowel ×
- ☐ Diffuse large B cell lymphoma ×

Submit answer

Reference ranges 

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The lymph node biopsied lacks a mantle zone and is made up of a predominant population of centrocytes with few tangible body macrophages. Immunohistochemistry confirms strong positivity for CD20 as well as CD70a, CD10, BCL2 and BCL6. The proliferation index (Ki-67) is low, no more than 20%.

What is the most likely diagnosis?

Nodular sclerosing lymphoma	16%
Lymphoplasmacytic lymphoma	12%
Follicular lymphoma	32%
Adenocarcinoma of the large bowel	2%
Diffuse large B cell lymphoma	39%

The correct answer here can be worked out based on the Ki-67 index. This is the proliferation index and is a marker (antigen) of the cancer cells metabolic rate. In high grade lymphomas such as diffuse large B cell lymphoma the Ki-67 will be high (>45%) therefore answer 5 is wrong. In low grade lymphomas such as follicular lymphoma the Ki-67 is low (<40%).

Follicular lymphoma (a form of non Hodgkin's lymphoma) often presents as incidentally found enlarged lymph nodes and may present without the B symptoms often seen in Hodgkin's lymphoma. It can undergo a transformation at any stage into a high grade lymphoma.

Answer 1 is wrong because as it is a form of Hodgkin's lymphoma the histology report would have mentioned the presence of reed-sternberg cells. Answer 2 is Waldenstrom's macroglobulinemia and presents with an IgM gammopathy. Answer 4 is wrong because an adenocarcinoma of the large bowel would have most likely been seen on a CT scan.

Non-Hodgkin's lymphoma ★

Lymphoma is the malignant proliferation of lymphocytes which accumulate in lymph nodes or other organs. Lymphoma may be classified as either Hodgkin's lymphoma (a specific type of lymphoma characterized by the presence of Reed-Sternberg cells) or non-Hodgkin's lymphoma (every other type of lymphoma that is not Hodgkin's lymphoma). Non-Hodgkin's lymphoma is the 6th most common cause of cancer in the UK. Non-Hodgkin's lymphoma may affect either B or T-cells and can be further classified as high grade or low grade.

Epidemiology

- Non-Hodgkin's lymphoma is much more common than Hodgkin's lymphoma
- While different subtypes can affect different ages, it typically affects the elderly with one-third of cases occurring in those over 75 years of age
- The incidence rate is 28 for men and 20 for females per 100,000 of the population

Risk factors

- Elderly
- Caucasians
- History of viral infection (specifically Epstein-Barr virus)
- Family history
- Certain chemical agents (pesticides, solvents)
- History of chemotherapy or radiotherapy
- Immunodeficiency (transplant, HIV, diabetes mellitus)
- Autoimmune disease (SLE, Sjogren's, coeliac disease)

Clinical presentation

Symptoms

- Painless lymphadenopathy (non-tender, rubbery, asymmetrical)
- Constitutional/B symptoms (fever, weight loss, night sweats, lethargy)
- Extranodal Disease - gastric (dyspepsia, dysphagia, weight loss, abdominal pain), bone marrow (pancytopenia, bone pain), lungs, skin, central nervous system (nerve palsies)

While differentiating Hodgkin's lymphoma from non-Hodgkin's lymphoma is done by biopsy certain elements of the clinical presentation can help point towards one rather than the other.

- Lymphadenopathy in Hodgkin's lymphoma can experience alcohol-induced pain in the node
- 'B' symptoms typically occur earlier in Hodgkin's lymphoma and later in non-Hodgkin's lymphoma
- Extra-nodal disease is much more common in non-Hodgkin's lymphoma than in Hodgkin's lymphoma

Signs

- Signs of weight loss
- Lymphadenopathy (typically in the cervical, axillary or inguinal region)
- Palpable abdominal mass - hepatomegaly, splenomegaly, lymph nodes
- Testicular mass
- Fever

Investigations

Investigations

- Excisional node biopsy is the diagnostic investigation of choice (certain subtypes will have a classical appearance on biopsy such as Burkitt's lymphoma having a 'starry sky' appearance)
- CT chest, abdomen and pelvis (to assess staging)
- HIV test (often performed as this is a risk factor for non-Hodgkin's lymphoma)
- FBC and blood film (patient may have a normocytic anaemia and can help rule out other haematological malignancy such as leukaemia)
- ESR (useful as a prognostic indicator)
- LDH (a marker of cell turnover, useful as a prognostic indicator)
- Other investigations can be ordered as the clinical picture indicates (LFT's if liver metastasis suspected, PET CT or bone marrow biopsy to look for bone involvement, LP if neurological symptoms)

Staging

Lugano staging

- Stage I: Involvement of a single lymph node region (I) or a single extralymphatic organ or site (IE).
- Stage II: Involvement of two or more lymph node regions on the same side of the diaphragm (II) or localized involvement of an extralymphatic organ or site and one or more lymph node regions on the same side of the diaphragm (IIE).
- Stage III: Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of an extralymphatic organ or site (IIIE), involvement of the spleen (IIIS), or both (IIIE+S).
- Stage IV: Diffuse or disseminated involvement of one or more extralymphatic organs, with or without associated lymph node involvement.

In addition to these stages, the classification includes the following:

- A/B Symptom Designation: The absence of significant symptoms is designated as 'A', while the presence of fever, night sweats, or weight loss is designated as 'B'.
- E: The presence of extranodal disease is denoted by the letter 'E'.
- S: Involvement of the spleen is denoted by the letter 'S'.
- X: Bulky disease (large tumor mass) is denoted by the letter 'X'.

The Lugano classification also emphasizes the role of PET scans in determining the stage of the disease, particularly in assessing whether the lymphoma is metabolically active in different parts of the body.

Management

Management

- Management is dependent on the specific sub-type of non-Hodgkin's lymphoma and will typically take the form of watchful waiting, chemotherapy or radiotherapy.
 - Rituximab is used in combination with conventional chemotherapy regimes (e.g. CHOP) for a variety of types of NHL

+ All patients should be screened for hepatitis B (HBV) before treatment with rituximab as it can cause reactivation of HBV in patients with prior exposure

+ Patients should also be monitored for cytopenias during treatment

- All patients will receive flu/pneumococcal vaccines
- Patients with neutropenia may require antibiotic prophylaxis

Complications

- Bone marrow infiltration causing anaemia, neutropenia or thrombocytopenia
- Superior vena cava obstruction
- Metastasis
- Spinal cord compression
- Complications related to treatment e.g. Side effects of chemotherapy

Prognosis

- Low-grade non-Hodgkin's lymphoma has a better prognosis
- High-grade non-Hodgkin's lymphoma has a worse prognosis but a higher cure rate



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[Haematological cancers - recognition and referral](#)

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Media



[Non-Hodgkin's lymphoma](#)

Osmosis - YouTube

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[Non-Hodgkin's lymphoma](#)

Medicosis Perfectionalis - YouTube

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Question 7 of 89



A 72-year-old woman presents to the emergency department following a fall. On examination, her right leg is shortened and externally rotated and she is unable to weight bear. A hip X-ray demonstrates a fractured neck of femur which appears pathological. She has no history of cancer. Following a dynamic hip screw insertion, she recovers well. She has blood tests sent for FBC, U&E, LDH, calcium, albumin, uric acid, serum electrophoresis, immunoglobulins and ESR. She has had a chest X-ray which was normal.

What additional tests should be requested to complete the initial investigations of the pathological nature of the fracture?

- | | |
|---|---|
| <input type="radio"/> MRI whole spine | × |
| <input type="radio"/> MRI hip | × |
| <input type="radio"/> Urinary electrophoresis | × |
| <input type="radio"/> Trephine biopsy | × |
| <input type="radio"/> Bone marrow biopsy | × |

Submit answer

Reference ranges ▾

Score: **0%**

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A 72-year-old woman presents to the emergency department following a fall. On examination, her right leg is shortened and externally rotated and she is unable to weight bear. A hip X-ray demonstrates a fractured neck of femur which appears pathological. She has no history of cancer. Following a dynamic hip screw insertion, she recovers well. She has blood tests sent for FBC, U&E, LDH, calcium, albumin, uric acid, serum electrophoresis, immunoglobulins and ESR. She has had a chest X-ray which was normal.

What additional tests should be requested to complete the initial investigations of the pathological nature of the fracture?

MRI whole spine	32%
MRI hip	12%
Urinary electrophoresis	46%
Trephine biopsy	3%
Bone marrow biopsy	7%

The correct answer answer is urinary eletrophoresis. This is a patient with a pathological fracture and at high risk of myeloma and needs to be fully investigated.

The following tests are needed to complete a myeloma screen:

- FBC, ESR, U&E, calcium, albumin, uric acid
- Serum protein electrophoresis
- Urine protein electrophoresis
- Immunoglobulin levels
- Plain X-ray of symptomatic areas

If initial investigations are suggestive of myeloma then bone marrow aspirate and trephine biopsies are indicated, as well as immunofixation of the serum and urine to demonstrate the nature of the paraprotein.

MRI would be contra-indicated due to the recent operation.

Source:



Discuss (17)

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Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
 - much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
 - this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection

- a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)

- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



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NICE



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[2016 myeloma guidelines](#)

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Media



Multiple Myeloma - Diagnosis and Treatment

Medicosis Perfectionalis - YouTube

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Multiple Myeloma

Medicosis Perfectionalis - YouTube

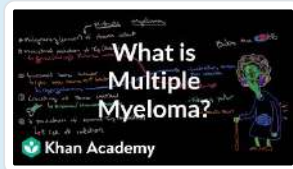
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Multiple Myeloma Mnemonic...the story of the plasma cell

Medicosis Perfectionalis - YouTube

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What is multiple myeloma?

Khan Academy - YouTube

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Multiple Myeloma

Townsend Teaching - YouTube

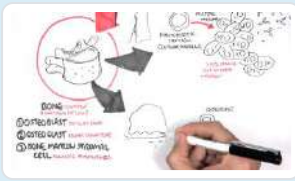
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Multiple Myeloma

CRASH! Medical Review - YouTube

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Multiple Myeloma

Armando Hasudungan - YouTube

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A 30-year-old gentleman presents with acute lethargy and shortness of breath. He reports cutting his leg on a wooden splinter in a bench with a red area that arose in the leg and spread rapidly. Two days later his leg remained painful and he started to develop chills and was brought into the hospital by concerned family.

On examination, he is pale and clammy with a capillary refill time of 4 seconds. His chest is clear but his breathing is shallow and rapid. His heart rate is 123 beats/min and is regular while his blood pressure is 85/65 mmHg. His leg shows the cut which is now raised and red-purple with a collection of pus under the skin. His cannula site is oozing blood. He receives three litres of intravenous fluid and is started on vancomycin and gentamicin intravenously.

Hb	130 g/l
Platelets	$110 \times 10^9/l$
WBC	$34.0 \times 10^9/l$
CRP	459 ng/ml
PT	18 seconds
APTT	45 seconds
Fibrinogen	0.1
Chest x-ray	patchy bilateral infiltrates
Wound swab	<i>Streptococcus pyogenes</i>

What is the explanation of the coagulation?

- ☐ Disseminated intravascular coagulopathy (DIC) ×
- ☐ Activation of thrombin by insect venom ×
- ☐ Haemodilution by intravenous fluids ×
- ☐ Haemophilia A ×
- ☐ Von Willebrand disease ×

Submit answer

Score: 0%	
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A 30-year-old gentleman presents with acute lethargy and shortness of breath. He reports cutting his leg on a wooden splinter in a bench with a red area that arose in the leg and spread rapidly. Two days later his leg remained painful and he started to develop chills and was brought into the hospital by concerned family.

On examination, he is pale and clammy with a capillary refill time of 4 seconds. His chest is clear but his breathing is shallow and rapid. His heart rate is 123 beats/min and is regular while his blood pressure is 85/65 mmHg. His leg shows the cut which is now raised and red-purple with a collection of pus under the skin. His cannula site is oozing blood. He receives three litres of intravenous fluid and is started on vancomycin and gentamicin intravenously.

Hb	130 g/l
Platelets	$110 \times 10^9/l$
WBC	$34.0 \times 10^9/l$
CRP	459 ng/ml
PT	18 seconds
APTT	45 seconds
Fibrinogen	0.1
Chest x-ray	patchy bilateral infiltrates
Wound swab	<i>Streptococcus pyogenes</i>

What is the explanation of the coagulation?


Disseminated intravascular coagulopathy (DIC)	91%
Activation of thrombin by insect venom	3%
Haemodilution by intravenous fluids	1%
Haemophilia A	2%
Von Willebrand disease	3%

Deranged coagulation in sepsis -> DIC

Important for me Less important

This patient is acutely septic and has deranged coagulation. Haemodilution would not deplete fibrinogen severely. Haemophilia A and Von Willebrand disease have a mildly raised APTT only but normal fibrinogen level. There is no history of an insect bite making it unlikely.

DIC is a consequence of severe sepsis where the clotting cascade is activated throughout the body forming small thrombus throughout the body but depleting the clotting factors. Specifically, there is a low fibrinogen. There are rare cases of snake venom activating the clotting cascade in a manner similar to DIC but there is no recall of a snake and is rare in the UK.

		 Discuss (4)	Improve
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Next question >

Disseminated intravascular coagulation ★

Under homeostatic conditions, coagulation and fibrinolysis are coupled. The activation of the coagulation cascade yields thrombin that converts fibrinogen to fibrin; the stable fibrin clot being the final product of hemostasis. The fibrinolytic system breaks down fibrinogen and fibrin. Activation of the fibrinolytic system generates plasmin (in the presence of thrombin), which is responsible for the lysis of fibrin clots. The breakdown of fibrinogen and fibrin results in polypeptides (fibrin degradation products). In a state of homeostasis, the presence of plasmin is critical, as it is the central proteolytic enzyme of coagulation and is also necessary for fibrinolysis.

In DIC, the processes of coagulation and fibrinolysis are dysregulated, and the result is widespread clotting with resultant bleeding. Regardless of the triggering event of DIC, once initiated, the pathophysiology of DIC is similar in all conditions. One critical mediator of DIC is the release of a transmembrane glycoprotein (tissue factor = TF). TF is present on the surface of many cell types (including endothelial cells, macrophages, and monocytes) and is not normally in contact with the general circulation, but is exposed to the circulation after vascular damage. For example, TF is released in response to exposure to cytokines (particularly interleukin 1), tumour necrosis factor, and endotoxin. This plays a major role in the development of DIC in septic conditions. TF is also abundant in tissues of the lungs, brain, and placenta. This helps to explain why DIC readily develops in patients with extensive trauma. Upon activation, TF binds with coagulation factors that then triggers the extrinsic pathway (via Factor VII) which subsequently triggers the intrinsic pathway (XII to XI to IX) of coagulation.

Causes of DIC

- sepsis
- trauma
- obstetric complications e.g. amniotic fluid embolism or hemolysis, elevated liver function tests, and low platelets (HELLP syndrome)
- malignancy

Diagnosis

A typical blood picture includes:

- ↓ platelets
- ↓ fibrinogen
- ↑ PT & APTT
- ↑ fibrinogen degradation products
- schistocytes due to microangiopathic haemolytic anaemia


Disorder	Prothrombin time	APTT	Bleeding time	Platelet count
Warfarin administration	Prolonged	Normal	Normal	Normal
Aspirin administration	Normal	Normal	Prolonged	Normal
Heparin	Often normal (may be prolonged)	Prolonged	Normal	Normal
DIC	Prolonged	Prolonged	Prolonged	Low

 + Q 123 

Next question >


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Textbooks

High-yield textbook

Extended textbook

Media



Disseminated intravascular coagulation

Osmosis - YouTube



2



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[Report broken media](#)

Score: **16.7%**

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Question 9 of 89



A patient has been admitted with left lower limb deep vein thrombosis. He was diagnosed by the FY1 who has efficiently started him on warfarin.

Two days after initiation you are asked to see this gentleman who has developed skin necrosis over his right thigh.

What is the most likely cause of his skin necrosis?

- ☐ Antiphospholipid syndrome ×
- ☐ Heparin induced thrombocytopenia (HIT) type II ×
- ☐ Excessive serum Antithrombin III ×
- ☐ Acquired haemophilia ×
- ☐ Protein C deficiency ×

Submit answer

Reference ranges 

Score: **0%**

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Question 9 of 89



A patient has been admitted with left lower limb deep vein thrombosis. He was diagnosed by the FY1 who has efficiently started him on warfarin.

Two days after initiation you are asked to see this gentleman who has developed skin necrosis over his right thigh.

What is the most likely cause of his skin necrosis?

Antiphospholipid syndrome	2%
Heparin induced thrombocytopenia (HIT) type II	6%
Excessive serum Antithrombin III	9%
Acquired haemophilia	2%
Protein C deficiency	82%

Answer: Protein C deficiency.

Warfarin induced skin necrosis is rare but very severe.

Be reminded that warfarin inhibits production of the vitamin K dependent coagulation factors including factors II, VII, IX and X but also the natural anticoagulants, proteins C and S. The first factors affected by warfarin are the anticoagulants, making warfarin temporarily pro-thrombotic during induction, in its initial few days of use and that is why it is advised to start heparin concurrently with Warfarin.

Various theories have been postulated as to the cause of this problem one of which is a background of congenital or acquired protein C, S or Antithrombin III deficiency.

Antithrombotic therapy for atrial fibrillation BMJ 2002; 325 doi:
<http://dx.doi.org/10.1136/bmj.325.7371.1022> (Published 02 November 2002)

Cite this as: BMJ 2002;325:1022 <http://www.bmj.com/rapid-response/2011/10/29/warfarin-induced-skin-necrosis>

Coumadin-Induced Skin Necrosis Janice M. Beitz, PhD, RN, CS, CNOR, CWOCN
<http://www.medscape.com/viewarticle/4431264>

Next question >

Protein C deficiency ★

Protein C deficiency is an autosomal codominant condition which causes an increased risk of thrombosis

Features

- venous thromboembolism
- skin necrosis following the commencement of warfarin: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis

 + Q 123 


Next question >

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Textbooks

High-yield textbook



Extended textbook



Links

Rare Disease Video Library - NORD

Protein C and Protein S Deficiency

DermnetNZ

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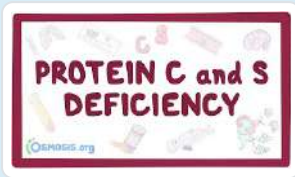
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Warfarin induced skin necrosis



[Suggest link](#)

[Report broken link](#)

Media



[Protein C and S deficiency](#)

Osmosis - YouTube  4  0

[Report broken media](#)

Score: **16.7%**

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Question 10 of 89



A 38-year-old female presents to the emergency department with pain in her right leg, which she attributes to tripping up and landing on the floor when she went hiking with her boyfriend approximately 1 week ago. She does not recall any insect bites but has become increasingly concerned as her leg has become more swollen and tender in the calf region.

She has no significant medical history but has been recovering from an episode of pneumonia for which her GP prescribed her clarithromycin. Her only other medication is the oral contraceptive pill which she started about 1 month ago. She consumes alcohol socially at the weekends and smokes approximately 10-15 cigarettes a day. On physical exam she is afebrile and her other vital signs are within normal limits. She is able to ambulate in the emergency department without significant issues, and there are no obvious skin breakages or significant bony deformities. You note that her left leg is significantly swollen compared to the right leg and there is evidence of pitting oedema and erythema. Passive dorsiflexion of her left foot leads to significant pain.

What is the next best step in the management of this patient?

- ☐ Obtain a doppler ultrasound scan of her left lower limb ×
- ☐ D-dimer test ×
- ☐ Start her empirically on oral amoxicillin for probable lower limb cellulitis ×
- ☐ X-ray her left tibial and fibula ×
- ☐ Reassure her and advise her to take regular paracetamol ×

Submit answer

Reference ranges 

Score: **0%**

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Question 10 of 89



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What is the next best step in the management of this patient?

Obtain a doppler ultrasound scan of her left lower limb	84%
D-dimer test	11%
Start her empirically on oral amoxicillin for probable lower limb cellulitis	2%
X-ray her left tibial and fibula	2%
Reassure her and advise her to take regular paracetamol	1%

If a 2-level DVT Wells score is ≥ 2 points then arrange a proximal leg vein ultrasound scan within 4 hours

Important for me Less important


This patient most likely has a left lower limb deep vein thrombosis. Her important risk factors include the fact that she is taking the oral contraceptive pill and is a smoker, which combined leads to a significantly increased risk for venous thromboembolic complications. In fact, smoking is a contraindication to starting the oral contraceptive pill in females greater than the age of 35 years. In addition, physical exam findings are also concerning for a deep vein thrombosis. Although we could start investigating her by doing a D-dimer test, if this is normal she still has a high pretest probability of deep vein thrombosis and we could therefore not confidently exclude this diagnosis. Consequently, the best way to confirm or refute a diagnosis of deep vein thrombosis, in this case, would be obtaining a Doppler ultrasound scan of her leg.

A D-dimer would not necessarily be wrong, but even if this returned as normal she is at considerable risk of deep vein thrombosis and should have a doppler ultrasound scan done anyway. In addition, she is being treated for pneumonia which is likely to confound the results of the D-dimer test anyway.

Although she does have swelling and erythema of her lower limb, she is afebrile and her clinical picture does not fit that of cellulitis.

She is ambulant and is unlikely to have sustained any significant bony injuries to her tibia and fibula, particularly as the mechanism of her injury was not very severe. Fractures of the tibia/fibula typically require a more significant mechanism of injury such as motor vehicle accidents.

It would be inappropriate to reassure her and advised her to take regular analgesia, as she is at significant risk of deep vein thrombosis and this needs to be excluded first.

   Discuss (6) [Improve](#)

[Next question >](#)

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1

Clinical feature	Points
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)
 - interim therapeutic anticoagulation used to mean giving low-molecular weight heparin
 - NICE updated their guidance in 2020. They now recommend using an anticoagulant that can be continued if the result is positive.
 - this means normally a direct oral anticoagulant (DOAC) such as apixaban or rivaroxaban
- if the scan is negative but the D-dimer is positive:
 - stop interim therapeutic anticoagulation
 - offer a repeat proximal leg vein ultrasound scan 6 to 8 days later

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test
 - this should be done within 4 hours. If not, interim therapeutic anticoagulation should be given until the result is available
 - if the result is negative then DVT is unlikely and alternative diagnoses should be considered
 - if the result is positive then a proximal leg vein ultrasound scan should be carried out within 4 hours

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer

at increased risk

- an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



123



Next question >

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Textbooks

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Links

NICE

5 0

[2020 Venous thromboembolism guidelines](#)

[Suggest link](#)

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Media



Deep vein thrombosis

Osmosis - YouTube

👍 3 👎 0



Understanding Deep Vein Thrombosis (DVT)

Zero To Finals - YouTube

👍 2 👎 1



Deep Vein Thrombosis - Overview (pathophysiology, treatment, complications)

Armando Hasudungan - YouTube

👍 3 👎 2

[Report broken media](#)

Score: **16.7%**

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Question 11 of 89



A 51-year-old man is investigated for a chronic cough, chest pain and dyspnoea. He also reports some difficult swallowing bread and meat for the past two weeks. He has no past medical history of note although has smoked for the past 30 years.

A CT scan is requested:



© Image used on license from Radiopaedia



What is the most likely diagnosis?

- | | |
|--|---|
| <input type="radio"/> Sarcoidosis | × |
| <input type="radio"/> Lung cancer | × |
| <input type="radio"/> Cardiac myxoma | × |
| <input type="radio"/> Oesophageal cancer | × |
| <input type="radio"/> Thymoma | × |

Submit answer

Reference ranges ▾

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Question 11 of 89



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A CT scan is requested:



© Image used on license from Radiopaedia



What is the most likely diagnosis?

Sarcoidosis	2%
Lung cancer	13%
Cardiac myxoma	8%
Oesophageal cancer	9%
Thymoma	67%

The CT slice at the bifurcation of the main bronchus shows an invasive thymoma presenting as an anterior mediastinal mass.

The differential diagnosis of an anterior mediastinal mass includes:

- thymoma
- lymphoma
- thyroid and parathyroid malignancies
- germ cell tumours e.g. teratomas
- thoracic aortic aneurysm



Discuss (8)

Improve

Next question >

Thymoma ★

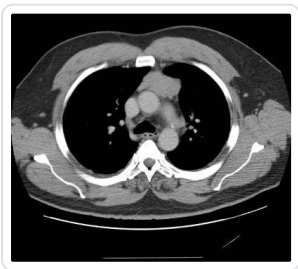
Thymomas are the most common tumour of the anterior mediastinum and is usually detected between the sixth and seventh decades of life.

Associated with

- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH





Causes of death

- compression of airway
- cardiac tamponade



123



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Textbooks

High-yield textbook

Extended textbook

Links

Radiopaedia














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[Thymic tumours](#)

[Suggest link](#)

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Score: **16.7%**

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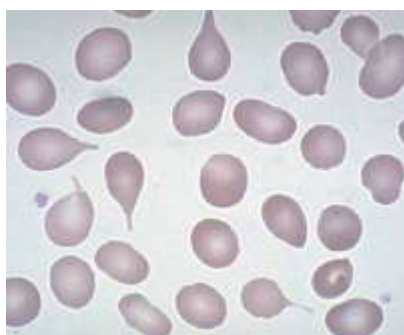


Question 12 of 89



A 77-year-old man is referred to haematology for investigation of anaemia. For several months he has been complaining of fatigue and weight loss. His GP has already arranged upper and lower gastrointestinal (GI) endoscopy which has been reported as normal.

His blood film is shown below:



What is the most likely diagnosis?

- ☐ Chronic lymphocytic leukaemia ×
- ☐ Myelofibrosis ×
- ☐ Iron deficiency anaemia (bleeding from non-GI source) ×
- ☐ Hyposplenism ×
- ☐ Autoimmune hemolytic anaemia ×

Submit answer

Reference ranges ▾

Score: **0%**

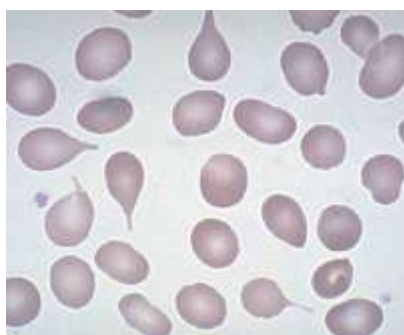
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A 77-year-old man is referred to haematology for investigation of anaemia. For several months he has been complaining of fatigue and weight loss. His GP has already arranged upper and lower gastrointestinal (GI) endoscopy which has been reported as normal.

His blood film is shown below:



What is the most likely diagnosis?

Chronic lymphocytic leukaemia

4%

Myelofibrosis

84%

Iron deficiency anaemia (bleeding from non-GI source)

6%

Hyposplenism

5%

Autoimmune hemolytic anaemia

1%

The blood film shows the typical 'tear-drop' poikilocytes of myelofibrosis.



Discuss (3)

Improve

Next question >

Myelofibrosis ★

Overview

- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes

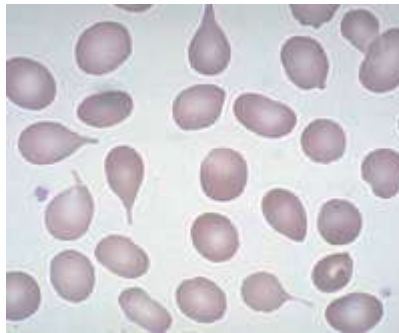
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

Features

- e.g. elderly person with symptoms of anaemia e.g. fatigue (the most common presenting symptom)
- massive splenomegaly
- hypermetabolic symptoms: weight loss, night sweats etc

Laboratory findings

- anaemia
- high WBC and platelet count early in the disease
- 'tear-drop' poikilocytes on blood film
- unobtainable bone marrow biopsy - 'dry tap' therefore trephine biopsy needed
- high urate and LDH (reflect increased cell turnover)



Blood film showing the typical 'tear-drop' poikilocytes of myelofibrosis



123



Next question >

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Links

British Journal of Haematology

👍 0 👎 1

[Use of JAK inhibitors in the management of myelofibrosis](#)

[Suggest link](#)

[Report broken link](#)

Media



[Myelofibrosis](#)

Osmosis - YouTube

👍 7 👎 0



[Myelofibrosis](#)

Medicosis Perfectionalis - YouTube

👍 3 👎 1



[Myelofibrosis](#)

Armando Hasudungan - YouTube

👍 5 👎 2

[Report broken media](#)

Score: **16.7%**

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A 47-year-old man is referred to the respiratory clinic with a 3 month history of cough associated with retrosternal chest pain. A chest x-ray requested by his GP has been reported as abnormal.

The chest x-ray is shown below



© Image used on license from Radiopaedia



What is the most likely diagnosis?

- | | |
|--|---|
| <input type="radio"/> Oesophageal cancer | × |
| <input type="radio"/> Cardiac myxoma | × |
| <input type="radio"/> Thymoma | × |
| <input type="radio"/> Lung cancer | × |
| <input type="radio"/> Sarcoidosis | × |

Submit answer

Reference ranges ▾

Score: 0%	
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Question 13 of 89



A 47-year-old man is referred to the respiratory clinic with a 3 month history of cough associated with retrosternal chest pain. A chest x-ray requested by his GP has been reported as abnormal.

The chest x-ray is shown below



© Image used on license from Radiopaedia

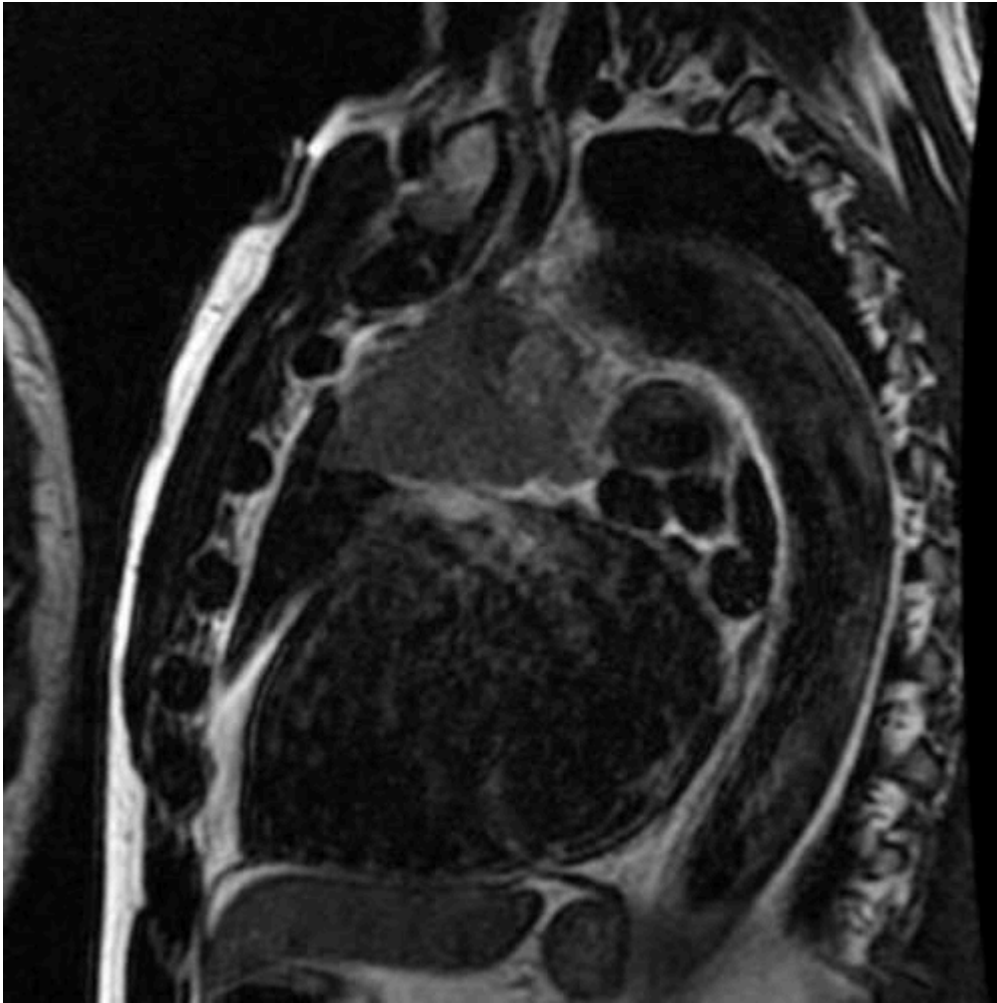


What is the most likely diagnosis?

Oesophageal cancer	2%
Cardiac myxoma	3%
Thymoma	85%
Lung cancer	4%
Sarcoidosis	5%

The chest x-ray demonstrates a soft tissue density projecting to the left of the mediastinum. The distal part of the arch and proximal descending aorta can be seen as separate suggesting it is located anterior to these structures.

A MRI scan from the same patient is shown below:



© Image used on license from Radiopaedia



MRI confirms the presence of an anterior mediastinal mass without convincing macroscopic invasion

		Discuss (7)	Improve
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Next question >

Thymoma ★

Thymomas are the most common tumour of the anterior mediastinum and is usually detected between the sixth and seventh decades of life.

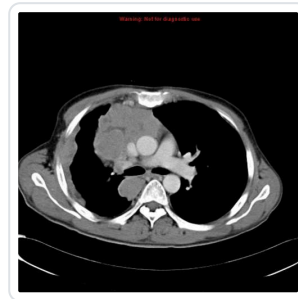
Associated with

- myasthenia gravis (30-40% of patients with thymoma)

- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death

- compression of airway
- cardiac tamponade



123



Next question >

B

I



A



T



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Links

Radiopaedia

[Thymic tumours](#)



8



3

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Score: **16.7%**

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A 62-year-old woman presents to the haematology clinic. She has had lower back pain, which has been progressive in nature. She has also been noted to develop unexplained anaemia. Her initial protein electrophoresis and serum-free light chain assays raised suspicion of multiple myeloma. She has a past medical history of transient ischaemic attacks and hypertension. She takes clopidogrel, amlodipine and ramipril. What imaging should be offered to further assess her?

- ☐ Lumbosacral X-rays

×
- ☐ Skeletal survey

×
- ☐ Bone marrow ultrasound

×
- ☐ Whole body MRI

×
- ☐ PET scan

×

Submit answer

Reference ranges ▾

Score: 0%	
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Lumbosacral X-rays	2%
Skeletal survey	14%
Bone marrow ultrasound	0%
Whole body MRI	80%
PET scan	4%

The correct answer is whole body MRI. NICE advises that all patients suspected to have a diagnosis of myeloma should be offered whole body MRI as first-line imaging, and only consider whole body CT if the patient declines MRI or is unable to have it. Skeletal survey should only be considered if CT and MRI are both not possible. Fluorodeoxyglucose positron emission tomography CT (FDG PET CT) can be considered once a diagnosis is confirmed.

Source:

'Myeloma: diagnosis and management.' NICE guideline [NG35]. The National Institute for Health and Care Excellence, February 2016.



Discuss (1)
Improve

Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
 - much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
 - this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure

- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.

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Links

Clinical Knowledge Summaries

 10  10

[Haematological cancers - recognition and referral](#)

NICE

 12  6

[2016 myeloma guidelines](#)

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Media



[Multiple Myeloma - Diagnosis and Treatment](#)

Medicosis Perfectionalis - YouTube

 6  0



[Multiple Myeloma](#)

Medicosis Perfectionalis - YouTube

 4  0



[Multiple Myeloma Mnemonic...the story of the plasma cell](#)

Medicosis Perfectionalis - YouTube

👍 5 🗑️ 1



What is multiple myeloma?

Khan Academy - YouTube

👍 4 🗑️ 1



Multiple Myeloma

Townsend Teaching - YouTube

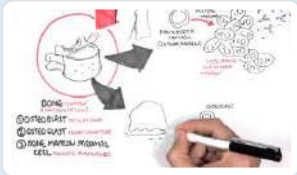
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Multiple Myeloma

CRASH! Medical Review - YouTube

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Multiple Myeloma

Armando Hasudungan - YouTube

👍 1 🗑️ 3

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Score: **16.7%**

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A 69-year-old gentleman presented for routine follow-up in the oncology clinic. He has metastatic poorly differentiated adenocarcinoma of unknown primary. He commenced palliative chemotherapy with oxaliplatin and fluorouracil two months ago. The most recent CT scan demonstrated stable disease.

Ten days ago he was admitted to the local emergency department with fever and diagnosed with neutropenic sepsis, of which the cause was not clear. He was admitted for IV Tazocin for five days then discharged with co-amoxiclav and filgrastim (G-CSF). He currently feels well. On examination, there are no abnormalities.

Observations:

Saturations	95%
Respiratory rate	14/min
Blood pressure	152/83mmHg
Heart rate	69/min
Temperature	37.3°C

Blood tests:

	14 days ago	Today
Hb	135g/l	124g/l
Platelets	322* 10 ⁹ /l	285* 10 ⁹ /l
WBC	0.2* 10 ⁹ /l	23.6* 10 ⁹ /l

What is the most appropriate course of action?

- ☐ Restart oral co-amoxiclav ×
- ☐ Arrange admission for IV tazocin ×
- ☐ Arrange admission for IV meropenem ×
- ☐ Start prednisolone ×
- ☐ Stop filgrastim (G-CSF) ×

Submit answer

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WBC	0.2* 10 ⁹ /l	23.6* 10 ⁹ /l

What is the most appropriate course of action?

Restart oral co-amoxiclav	2%
Arrange admission for IV tazocin	5%
Arrange admission for IV meropenem	5%
Start prednisolone	3%
Stop filgrastim (G-CSF)	86%

The correct answer is to stop filgrastim. Filgrastim stimulates a white cell count which can increase far above the normal range, and the white cell count will return to normal once it is stopped. The

key here is that the patient is clinically well, and further antibiotics are unnecessary.

Source:

Febrile Neutropenia.' BMJ Best Practice. N.p., 15 Sept. 2015.



Discuss (1)

Improve

Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



123

[Next question >](#)**B***I***A****T**

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Links

NICE

3 1

[2012 Neutropenic sepsis guidelines](#)

Christies

2 4

[2013 Neutropenic sepsis guidelines](#)[Suggest link](#)[Report broken link](#)

Media

[Febrile Neutropenia](#)

Townsend Teaching - YouTube

1 0



What is febrile neutropaenia (neutropenia)? - neutrophil function, pathophysiology, treatment

Armando Hasudungan - YouTube

👍 2 👎 1



Neutropenic sepsis

Oncology for Medical Students - YouTube

👍 5 👎 3

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Score: **16.7%**

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A 67-year-old female presents with 4-month history of increasing lethargy and malaise. She has no past medical history and travels widely, last visiting the Middle East one week prior to this admission, returning with a respiratory tract infection that appears to be resolving. She is a lifelong non-smoker and does not drink alcohol to excess. Over the past two weeks, she reports increasing bilateral persistent headache associated with binocular visual blurring. In addition, she describes a non-specific abdominal discomfort without any changes in bowel habit.

On examination, you note bilateral axillary lymphadenopathy and conjunctival pallor. Cardiovascular and respiratory system examinations were unremarkable. Neurological examination is unremarkable. Fundoscopy reveals dilated tortuous retinal veins. Abdominal examination reveals hepatosplenomegaly. Lastly, you note areas of purpura around her left anterior shin and her right upper arm. A chest radiograph is unremarkable.

Her blood results are as follows:

Hb	87 g/l
MCV	79 fl
Platelets	$190 \times 10^9/l$
WBC	$3.4 \times 10^9/l$
Na ⁺	142 mmol/l
K ⁺	4.5 mmol/l
Urea	7.6 mmol/l
Creatinine	89 μ mol/l
Adj Calcium	2.47 mmol/l
Phosphate	1.34 mmol/l
LDH	1890 (normal range 140-280 units/L)
Serum electrophoresis	IgM paraprotein band at 5.4 g/L

A bone marrow biopsy demonstrates 14% infiltration of lymphoplasmacytic cells

What is the most likely diagnosis?

☐ Waldenstrom's macroglobulinaemia



☐ Multiple myeloma



- ☐

Monoclonal gammopathy of unknown significance (MGUS)

×
- ☐

Chronic lymphocytic leukaemia (CLL)

×
- ☐

Upper respiratory tract infection (URTI)

×

Submit answer

Reference ranges ▾

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Serum electrophoresis	IgM paraprotein band at 5.4 g/L

A bone marrow biopsy demonstrates 14% infiltration of lymphoplasmacytic cells

What is the most likely diagnosis?

Waldenstrom's macroglobulinaemia	83%
Multiple myeloma	6%

Monoclonal gammopathy of unknown significance (MGUS)

8%

Chronic lymphocytic leukaemia (CLL)

3%

Upper respiratory tract infection (URTI)

0%

There is an enormous IgM paraprotein band on serum electrophoresis, immediately suggesting the differentials to narrow to Waldenstrom's macroglobulinaemia, multiple myeloma and MGUS. The patient is symptomatic, has bone marrow involvement of greater than 10% with IgM band greater than 3g/L, ruling out MGUS. The key to this diagnosis is differentiating between myeloma and Waldenstrom's: it is particularly rare (but not impossible) for an IgM-secreting plasma cell clone in myeloma but this accounts for only 0.5% of all multiple myelomas. Secondly, clinically, the patient demonstrates signs of hyperviscosity syndrome and splenomegaly, both of which are much more common in Waldenstrom's than myeloma. Thirdly, there is a lack of bone symptoms and renal involvement with normal serum calcium: bone lesions are significantly more common in multiple myeloma. Fourthly, fundoscopic tortuous and dilated veins are classical in hyperviscous patient with Waldenstrom's macroglobulinaemia. The diagnosis is clinched on bone marrow biopsy, demonstrating lymphoplasmacytic cells instead of plasma cells, confirmed by cell immunophenotyping.

CLL should not result in a paraprotein band, URTI may result in a rise in IgA but should not result in bone marrow involvement.



Discuss (8)

Improve

Next question >

Waldenstrom's macroglobulinaemia ★

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
 - the pentameric configuration of IgM increases serum viscosity
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Investigations

- monoclonal IgM paraproteinaemia

- bone marrow biopsy is diagnostic
 - infiltration of the bone marrow with lymphoplasmacytoid lymphoma cells

Management

- typically rituximab-based combination chemotherapy



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123



Next question >

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Waldenstrom's macroglobulinaemia

Medicosis Perfectionalis - YouTube 6 0





Waldenstrom's macroglobulinaemia

Osmosis - YouTube 5 0



What is Waldenstrom's macroglobulinaemia

Khan Academy Medicine - YouTube  0  0

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Score: **16.7%**

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A 34-year-old male presents with a 4 day history of bloody diarrhoea and vomiting, fevers and associated with occasional abdominal cramps. He reports no other symptoms. He reports no previous history of gastrointestinal disease; there is no family history of inflammatory bowel disease. He has no past medical history except for a left knee arthroscopy following an injury playing football 7 months ago. He is a lifelong non-smoker, drinks 14 units of alcohol a month, has not travelled abroad in the past year and last ate outside of his home a week ago during a barbecue at his brother's house.

On examination, he appears dehydrated. There is mild generalised abdominal tenderness with increased bowel sounds. Respiratory and cardiovascular examinations were unremarkable. His blood tests are as follows:

Hb	92 g/l
MCV	90fl
Platelets	$49 \times 10^9/l$
WBC	$14.2 \times 10^9/l$
Neutrophils	$12.8 \times 10^9/l$
Blood film	schistocytes, reticulocytosis
Direct antiglobulin test	negative
Urea	14.9 mmol/l
Creatinine	159 $\mu\text{mol/l}$
CRP	82 mg/l

What is the cause of this patient's blood abnormalities?

- ☐ Microangiopathic haemolytic anaemia ×
- ☐ Cold autoimmune haemolytic anaemia ×
- ☐ Warm autoimmune haemolytic anaemia ×
- ☐ Iron deficiency anaemia ×
- ☐ Acute myeloid leukaemia ×

Submit answer

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What is the cause of this patient's blood abnormalities?

Microangiopathic haemolytic anaemia	83%
Cold autoimmune haemolytic anaemia	6%
Warm autoimmune haemolytic anaemia	8%
Iron deficiency anaemia	0%
Acute myeloid leukaemia	3%

The first recognition in this patient is the underlying syndrome: blood film with fragment red cells (schistocytes), thrombocytopenia acute kidney injury, pyrexia and bloody diarrhoea, should

strongly suggest haemolytic uraemia syndrome-thrombotic thrombocytopenia purpura spectrum (HUS-TTP) in the absence of alternative unifying causes. In this case, gastrointestinal infection by *Campylobacter* from the recent barbecue, producing Shiga toxins and resulting in endothelial damage, is a strong possible culprit. The patient has a normocytic anaemia with red cell fragmentation and increased reticulocyte production, suggestive of rapid mechanical destruction and the bone marrow releasing immature red cells in (unsuccessful) compensation. This represents microangiopathic haemolytic anaemia (MAHA) in the context of HUS-TTP.

Both cold and warm autoimmune haemolytic anaemias should produce a positive direct antiglobulin test (Coombs): addition of a Coombs reagent containing antihuman globulin should agglutinate red cells IgM and IgG antibodies bound to in cold and warm autoimmune haemolytic anaemias respectively. Iron deficiency anaemia typically produces microcytic anaemias with target cells; there are no blast cells suggestive of leukaemia.

		 Discuss (3)	Improve
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Next question >

Haemolytic anaemias: by cause ★

Hereditary haemolytic anaemias can be subdivided into membrane, metabolism or haemoglobin defects

Hereditary causes

- membrane: hereditary spherocytosis/elliptocytosis
- metabolism: G6PD deficiency
- haemoglobinopathies: sickle cell, thalassaemia

Acquired haemolytic anaemias can be subdivided into immune and non-immune causes

Acquired: immune causes (Coombs-positive)

- autoimmune: warm/cold antibody type
- alloimmune: transfusion reaction, haemolytic disease newborn
- drug: methyldopa, penicillin

Acquired: non-immune causes (Coombs-negative)

- microangiopathic haemolytic anaemia (MAHA): TTP/HUS, DIC, malignancy, pre-eclampsia
- prosthetic heart valves
- paroxysmal nocturnal haemoglobinuria
- infections: malaria
- drug: dapsone

- Zieve syndrome
 - rare clinical syndrome of Coombs-negative haemolysis, cholestatic jaundice, and transient hyperlipidaemia associated with heavy alcohol use, typically following a binge
 - typically resolves with abstinence from alcohol



123



Next question >

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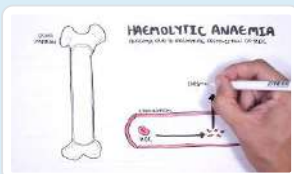


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[Haemolytic Anaemia - classification \(intravascular, extravascular\), pathophysiology, investigations](#)

Armando Hasudungan - YouTube



3



2

[Report broken media](#)

Score: **16.7%**

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A 23-year-old medical student went to Uganda on his elective but has had to return to the UK early due to illness. He had been careful to take malaria prophylaxis and slept under a mosquito net. He was using primaquine due to previous intolerable side effects with doxycycline. He was complaining of central abdominal pain and had noticed jaundiced sclera in the few days prior to returning to the UK. There is no relevant past medical history and he takes no regular medication. He is a non-smoker and drinks 2-4 units of alcohol weekly.

Observations show a blood pressure of 110/73 mmHg and heart rate of 98 beats per minute. He is afebrile, has a respiratory rate of 16 per minute and oxygen saturations of 94% on room air.

On examination, he is pale and jaundiced with yellow sclera. There is no cyanosis. His chest sounds clear and heart sounds are normal with nil added. The abdomen is soft, generally tender but with no guarding or peritonism. Bowel sounds are normal.

Bloods show the following:

Haemoglobin	86 g/L	Sodium	139 mmol/L
Platelets	188 x10 ⁹ /L	Potassium	3.6 mmol/L
White cell count	11.0 x10 ⁹ /L	Urea	3.0 mmol/L
Neutrophils	8.5 x10 ⁹ /L	Creatinine	62 micromol/L
Reticulocytes	11%	Albumin	34 g/L
CRP	7 mg/L	Bilirubin	67 micromol/L
ALT	21 iu/L		
Alkaline Phosphatase	40 iu/L		

Peripheral blood film:

- Heinz bodies seen with methyl violet staining.
- Bite and blister cells also present.

What is the most likely diagnosis?

☐ G6PD deficiency
 ×

☐ *Plasmodium falciparum* infection
 ×

☐ *Mycoplasma pneumoniae*
×

☐ Hereditary spherocytosis ×

☐ Lead poisoning ×

Submit answer

Reference ranges ▾

Score: **0%**

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Alkaline Phosphatase	40 iu/L		

Peripheral blood film:

- Heinz bodies seen with methyl violet staining.
- Bite and blister cells also present.

What is the most likely diagnosis?

G6PD deficiency	93%
<i>Plasmodium falciparum</i> infection	2%
<i>Mycoplasma pneumoniae</i>	1%

This student has acute haemolytic anaemia (anaemia, reticulocytosis and raised bilirubin with normal ALT). Answers A, C, D and E are all causes of haemolytic anaemia.

The blood film is the main diagnostic tool to differentiate between these answers. Heinz bodies, bite and blister cells are all seen in acute haemolysis associated with G6PD deficiency. The acute haemolysis has been triggered by antimalarial treatment (usually primaquine).

A blood film of hereditary spherocytosis shows spherocytes and reticulocytes. In lead poisoning, there should be dimorphic cells with ring granules on Perl's staining.

Plasmodium falciparum is a common form of malaria that multiplies in the liver. Infection with this can cause anaemia with abnormal liver function tests (LFTs). Persons with G6PD deficiency are somewhat protected from infection with *Plasmodium falciparum* and *Plasmodium vivax* malaria.

G6PD deficiency is X-linked and is more prevalent in Mediterranean populations.



Discuss (3)

Improve

Next question >

G6PD deficiency ★

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in an X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

Pathophysiology

- G6PD is the first step in the pentose phosphate pathway, which converts glucose-6-phosphate → 6-phosphogluconolactone
 - this reaction also results in nicotinamide adenine dinucleotide phosphate (NADP) → NADPH
 - i.e. glucose-6-phosphate + NADP → 6-phosphogluconolactone + NADPH
- NADPH is important for converting oxidized glutathione back to its reduced form
- reduced glutathione protects red blood cells from oxidative damage by oxidants such as superoxide anion (O₂⁻) and hydrogen peroxide
- ↓ G6PD → ↓ reduced NADPH → ↓ reduced glutathione → increased red cell susceptibility to oxidative stress

Features

- neonatal jaundice is often seen
- intravascular haemolysis
- gallstones are common
- splenomegaly may be present
- Heinz bodies on blood films. Bite and blister cells may also be seen

Diagnosis is made by using a G6PD enzyme assay

- levels should be checked around 3 months after an acute episode of hemolysis, RBCs with the most severely reduced G6PD activity will have hemolysed → reduced G6PD activity → not be measured in the assay → false negative results

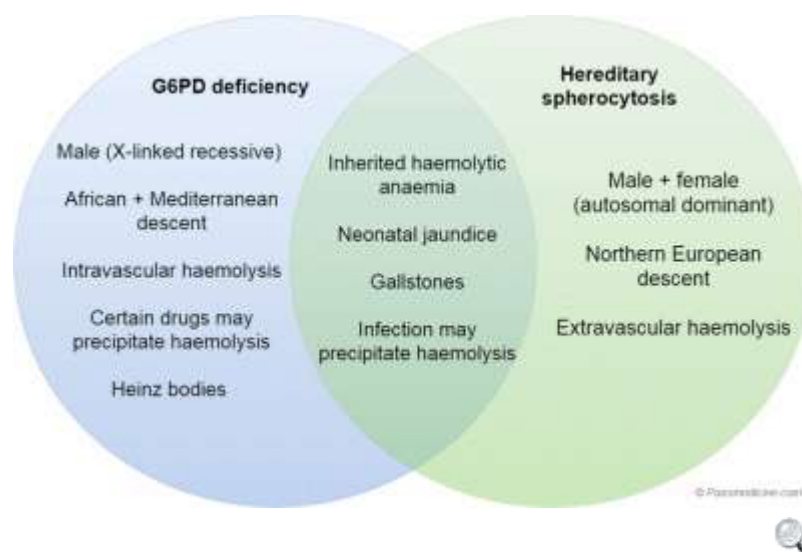
Some drugs causing haemolysis

- anti-malarials: primaquine
- ciprofloxacin
- sulph- group drugs: sulphonamides, sulphasalazine, sulfonylureas

Some drugs thought to be safe

- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

Comparing G6PD deficiency to hereditary spherocytosis:



Comparison of G6PD deficiency to hereditary spherocytosis

	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent
Typical history	<ul style="list-style-type: none"> • Neonatal jaundice • Infection/drugs precipitate haemolysis • Gallstones 	<ul style="list-style-type: none"> • Neonatal jaundice • Chronic symptoms although haemolytic crises may be precipitated by infection • Gallstones • Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	EMA binding



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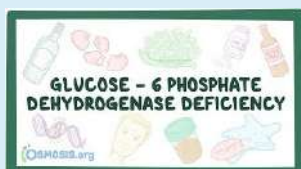

[Next question >](#)
B*I***A****T**

Textbooks

High-yield textbook

Extended textbook

Media



[Glucose-6-Phosphate Dehydrogenase \(G6PD\) deficiency](#)

Osmosis - YouTube



7



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Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

Medicosis Perfectionalis - YouTube

👍 2 🗑 0

[Report broken media](#)

Score: **16.7%**

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A 51-year-old man presents with dysuria and a low grade fever. He is prescribed a course of Nitrofurantoin for a suspected urinary tract infection. He has a history of ischaemic heart disease for which he takes aspirin and atorvastatin. The following day, he notices that his urine has become very dark and he feels breathless and more unwell.

Bloods show:

Hb	78 g/L
WCC	$14.1 \times 10^9/\text{L}$
Neutrophils	$13 \times 10^9/\text{L}$
Platelets	$280 \times 10^9/\text{L}$
Bilirubin	87 mg/dL
ALT	45 IU/L
Alkaline phosphatase	73 IU/L
Urea	5 mmol/L
Creatinine	80 $\mu\text{mol}/\text{L}$

Blood film microscopy comments on the presence of Heinz bodies. What is the underlying diagnosis?

- ☐ Hereditary spherocytosis ×
- ☐ Paroxysmal nocturnal haemoglobinuria ×
- ☐ Haemolytic uraemic syndrome ×
- ☐ Urinary sepsis secondary to *E. coli* ×
- ☐ Glucose-6-phosphate dehydrogenase deficiency (G6PD) ×

Submit answer

Reference ranges

Score: **0%**

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Blood film microscopy comments on the presence of Heinz bodies. What is the underlying diagnosis?

Hereditary spherocytosis

4%

Paroxysmal nocturnal haemoglobinuria

7%

Haemolytic uraemic syndrome

2%

Urinary sepsis secondary to *E. coli*

1%

Glucose-6-phosphate dehydrogenase deficiency (G6PD)

87%

The blood tests reveal anaemia with a bilirubin rise, which indicates haemolytic anaemia. Heinz bodies are red cell inclusions consisting of denatured Hb; they are a feature of oxidative stress. Nitrofurantoin is one of many drugs that can cause haemolytic crisis in G6PD deficiency. Heinz bodies would not usually be seen on the blood films of the other conditions.



Discuss (5)

Improve

G6PD deficiency ★

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in an X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

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Some drugs causing haemolysis

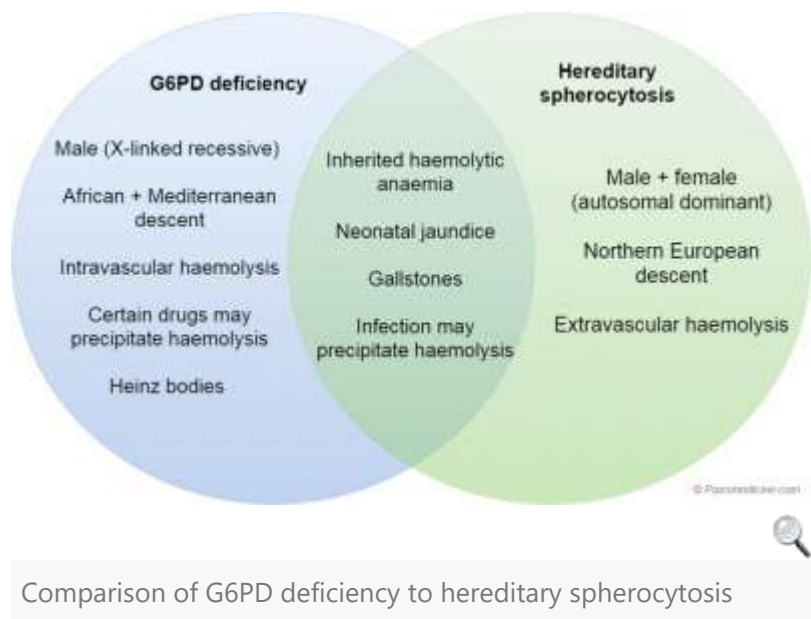
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Some drugs thought to be safe

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- cephalosporins
- macrolides

- tetracyclines
- trimethoprim

Comparing G6PD deficiency to hereditary spherocytosis:



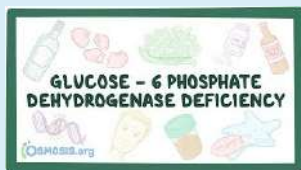
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Textbooks

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Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

Osmosis - YouTube

👍 7 👎 0



Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

Medicosis Perfectionalis - YouTube

👍 2 👎 0

[Report broken media](#)

Score: **16.7%**

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Question 20 of 89



A 26 year old female who is 14 days post-partum (spontaneous vaginal delivery) presents to your medical admissions unit with her partner who is worried that she is confused. She is unable to provide any history but her partner tells you that she has gradually gotten worse over the past few days. Her observations are as follows: temperature 38°C, pulse 90/min, blood pressure 154/88 mmHg, respiratory rate 16/min, sats 99% on room air.

On examination, she looks pale. Her chest is clear and abdomen is soft, non-tender. She has multiple bruises on her arms. Her blood results are pending.

What is the most likely diagnosis?

- ☐ Haemolytic uraemic syndrome ×
- ☐ Thrombotic thrombocytopenic purpura ×
- ☐ Idiopathic thrombocytopenic purpura ×
- ☐ Retained products of placenta ×
- ☐ Disseminated intravascular coagulation (DIC) ×

Submit answer

Reference ranges 

Score: **0%**

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On examination, she looks pale. Her chest is clear and abdomen is soft, non-tender. She has multiple bruises on her arms. Her blood results are pending.

What is the most likely diagnosis?

Haemolytic uraemic syndrome	2%
Thrombotic thrombocytopenic purpura	74%
Idiopathic thrombocytopenic purpura	3%
Retained products of placenta	4%
Disseminated intravascular coagulation (DIC)	16%

Thrombotic thrombocytopenic purpura is associated with fever, anaemia, thrombocytopenia, renal failure and confusion. Pregnancy and the post-partum state account for about 20% of cases seen.

Haemolytic uraemic syndrome is not associated with fever and confusion. Retained products of placental is more unlikely as her abdomen is soft, non-tender. DIC would be a differential diagnosis but is not the most likely diagnosis here. Idiopathic thrombocytopenic purpura would not cause confusion.



Discuss (6)
Improve

Next question >

Thrombotic thrombocytopenic purpura ★

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels

- in TTP there is a deficiency of ADAMTS13 (a metalloprotease enzyme) which breakdowns ('cleaves') large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Features

- rare, typically adult females
- fever
- fluctuating neuro signs (microemboli)
- microangiopathic haemolytic anaemia
- thrombocytopenia
- renal failure

Causes

- post-infection e.g. urinary, gastrointestinal
- pregnancy
- drugs: ciclosporin, oral contraceptive pill, penicillin, clopidogrel, aciclovir
- tumours
- SLE
- HIV



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

[2003 TTP/HUS guidelines](#)



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Media



Bleeding Disorders (ITP vs TTP vs HUS vs DIC)

Dirty USMLE - YouTube

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Report broken media

Score: **16.7%**

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A 52-year-old female with acute lymphoblastic leukaemia is on her third cycle of chemotherapy. She is admitted to the ward after developing a temperature of 38.7°C before her fourth cycle. She feels well in herself but has ongoing trouble with diarrhoea and mucositis. At present, her stools are type four on the Bristol stool chart and her mouth ulcers are being treated with a lidocaine/nystatin topical solution. She denies any cough, sore throat or urinary symptoms.

On examination, her abdomen is soft and non-tender with normal bowel sounds. Her chest is clear with air entry heard throughout. She has no murmurs, joint effusions or areas of cellulitis. Her mouth contains multiple ulcers with areas of straw colored exudate overlying them.

Hb	110 g/l
Platelets	$60 \times 10^9/l$
WBC	$1.1 \times 10^9/l$
Neuts	$0.5 \times 10^9/l$

Blood culture (1st)	<i>Staphylococcus epidermidis</i>
Blood culture (2nd)	no growth
Chest X-ray	clear lung fields, normal cardiac contour
Nasopharyngeal PCR	negative
Urine dip	negative for leucocytes and nitrites

Which investigation is most likely to elicit the cause of the fever?

- ☐ Sputum culture ×
- ☐ Urine culture ×
- ☐ Blood culture ×
- ☐ Stool sample ×
- ☐ Swab mouth ulcer ×

Submit answer

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Question 21 of 89



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Chest X-ray	clear lung fields, normal cardiac contour
Nasopharyngeal PCR	negative
Urine dip	negative for leucocytes and nitrites

Which investigation is most likely to elicit the cause of the fever?




Sputum culture	2%
Urine culture	2%
Blood culture	20%
Stool sample	17%
Swab mouth ulcer	59%

Mucositis can be a source of neutropenic sepsis

Important for me Less important

This patient has neutropenic sepsis of unknown source. In neutropenic patients, almost any site can be the source. From the history there is diarrhoea but her stools are currently normal. There are no urinary symptoms and the dipstick is normal making the urine unlikely to culture an organism. Ideally, three blood cultures should be completed in pyrexia of unknown origin so this is a useful suggestion. Sputum culture is impossible if there is no productive cough and would need to be induced by bronchoscopy.

Importantly, we are told there are mouth ulcers and this represents a break in the protective lining through which oral commensal bacteria can enter the blood stream and trigger sepsis. Therefore, a swab should be taken for bacterial culture and for viral PCR from the ulcer site.

		 Discuss (4)	Improve
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Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment

- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



123



Next question >

B

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Textbooks

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Links

NICE

👍 3 👎 1

[2012 Neutropenic sepsis guidelines](#)

Christies

👍 2 👎 4

[2013 Neutropenic sepsis guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Febrile Neutropenia](#)

Townsend Teaching - YouTube

👍 1 👎 0



What is febrile neutropaenia (neutropenia)? - neutrophil function, pathophysiology, treatment

Armando Hasudungan - YouTube

👍 2 👎 1



Neutropenic sepsis

Oncology for Medical Students - YouTube

👍 5 👎 3

[Report broken media](#)

Score: **16.7%**

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A 45-year-old lady presents to the Emergency Department progressive shortness of breath for the last three days. It is worse on activity but is not associated with any cough or wheeze. She has a past medical history of asthma and HIV, for which takes antiretroviral medication regularly. At her last clinic appointment two weeks ago, she was found to have oral candida and so was given a 2 week course of nystatin and started on dapsone for prophylaxis of pneumocystis jirovecii pneumonia. She is a non-smoker.

On examination, her lips and nail beds have a bluish tinge and she is visibly breathless. Her respiratory rate is 26 per minute and on pulse oximetry her saturations are 91% on air both at rest and on exercise. Her temperature is 36.5°C and she has not felt feverish. On auscultation she has vesicular breath sounds with minimal wheeze and normal heart sounds with no murmurs. She has no ankle oedema and JVP is not raised. There is no evidence of oral candidiasis and no lymphadenopathy. Her calves are soft and non-tender.

A chest x-ray shows clear lung fields with no focal consolidation or lymphadenopathy. ECG is sinus rhythm at 90 beats per minute with normal complexes throughout.

Arterial blood gas on air:

pH	7.51
PaO2	13.7 kPa
PaCO2	3.34 kPa
HCO3-	22.1 mmol/l
BE	-3.3 mmol/l
sO2	97%
Hb	113 g/l
Na+	143 mmol/l
K+	3.7 mmol/l
Glu	5.2 mmol/l
Lac	1.9 mmol/l

What is the most likely diagnosis?

- ☐ Acute asthma ×
- ☐ Carbon monoxide poisoning ×

<input type="radio"/>	Methemoglobinemia	×
<input type="radio"/>	Pneumocystis jirovecii pneumonia	×
<input type="radio"/>	Pulmonary embolus	×

Submit answer

Reference ranges ▾

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A 45-year-old lady presents to the Emergency Department progressive shortness of breath for the last three days. It is worse on activity but is not associated with any cough or wheeze. She has a past medical history of asthma and HIV, for which takes antiretroviral medication regularly. At her last clinic appointment two weeks ago, she was found to have oral candida and so was given a 2 week course of nystatin and started on dapsone for prophylaxis of pneumocystis jirovecii pneumonia. She is a non-smoker.

On examination, her lips and nail beds have a bluish tinge and she is visibly breathless. Her respiratory rate is 26 per minute and on pulse oximetry her saturations are 91% on air both at rest and on exercise. Her temperature is 36.5°C and she has not felt feverish. On auscultation she has vesicular breath sounds with minimal wheeze and normal heart sounds with no murmurs. She has no ankle oedema and JVP is not raised. There is no evidence of oral candidiasis and no lymphadenopathy. Her calves are soft and non-tender.

A chest x-ray shows clear lung fields with no focal consolidation or lymphadenopathy. ECG is sinus rhythm at 90 beats per minute with normal complexes throughout.

Arterial blood gas on air:

pH	7.51
PaO2	13.7 kPa
PaCO2	3.34 kPa
HCO3-	22.1 mmol/l
BE	-3.3 mmol/l
sO2	97%
Hb	113 g/l
Na+	143 mmol/l
K+	3.7 mmol/l
Glu	5.2 mmol/l
Lac	1.9 mmol/l

What is the most likely diagnosis?

- Acute asthma
2%
- Carbon monoxide poisoning
6%

Methemoglobinemia

85%

Pneumocystis jirovecii pneumonia

5%

Pulmonary embolus

3%

This lady has shortness of breath with low saturations on pulse oximetry but normal PaO₂ and saturations on arterial blood gas. This combined with a bluish discolouration and normal chest examination point towards a diagnosis of methemoglobinemia, a known side effect of the dapsone on which she has been started.

In exacerbation of asthma one would expect wheeze and a low PaO₂. Carbon monoxide poisoning typically results in cherry red appearance. This lady does not have any history of suggest pulmonary embolus and one would again expect a low PaO₂, associated with a tachycardia. Pneumocystis pneumonia would be unlikely on prophylaxis, and there may be x-ray changes and drop in saturations on exercise.

Reference: Prchal JT. Clinical features, diagnosis, and treatment of methemoglobinemia. Uptodate. Available online at: <http://www.uptodate.com/contents/clinical-features-diagnosis-and-treatment-of-methemoglobinemia>



Discuss (7)

Improve

Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe²⁺ to Fe³⁺. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe³⁺ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO₂ but decreased oxygen saturation

Management

- NADH methaemoglobinemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



123



Next question >

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Links

Life in the Fast Lane

6 3

[Methaemoglobinemia](#)

The Internet Book of Critical Care

10 4

[Methemoglobinemia](#)

[Suggest link](#)

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Media



Methaemoglobinaemia

Osmosis - YouTube 7 2

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A 44 year old female patient is admitted to the oncology ward to undergo chemotherapy for Diffuse Large B-Cell lymphoma stage IVb. She had originally presented to her GP with intermittent abdominal bloating and constipation and occasional shortness of breath. She also reported having to often get up in the middle of the night to change the bed clothes due to drenching sweats. Her GP had been concerned by these symptoms and had organised an immediate chest X-ray to be undertaken at the nearby hospital.

Chest X-ray

- large mediastinal mass with clear lung fields.

On receiving this report the GP arranged an urgent appointment with a local haematologist as he suspected that the patient was suffering from lymphoma. She was seen only 4 days later. Given the clinical history the team at the hospital arranged some urgent investigations.

Hb	9.5 g/dl
Platelets	140 * 10 ⁹ /l
WBC	36.5 * 10 ⁹ /l
Lactate Dehydrogenase	2540IU/l

CT-guided Lymph node biopsy

- cells are large, with prominent nucleoli and abundant cytoplasm and many mitoses expressing CD19 and CD20 markers

PET scan

- large extra-nodal disease bulks most notable in the ileo-caecal area and in the mediastinum. Overall bulky disease in keeping with the diagnosis of advanced stage lymphoma.

The patient is admitted to receive cycle one of R-CHOP chemotherapy under close monitoring.

What electrolyte abnormalities would suggest tumour lysis syndrome?

- ☐ High Potassium, high Calcium, low Phosphate ×
- ☐ Low Potassium, high Calcium, low Phosphate ×
- ☐ High Potassium, low Calcium, high Phosphate ×

- ☐ Low Potassium, low Calcium, high Phosphate
- ☐ Low Potassium, low Calcium, low Phosphate

Submit answer

Reference ranges ▾

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The patient is admitted to receive cycle one of R-CHOP chemotherapy under close monitoring.

What electrolyte abnormalities would suggest tumour lysis syndrome?

High Potassium, high Calcium, low Phosphate	12%
Low Potassium, high Calcium, low Phosphate	3%
High Potassium, low Calcium, high Phosphate	82%



Discuss (9)

Improve

[Next question >](#)

Tumour lysis syndrome ★

Tumour lysis syndrome (TLS) is a potentially deadly condition related to the treatment of high-grade lymphomas and leukaemias. It can occur in the absence of chemotherapy but is usually triggered by the introduction of combination chemotherapy. On occasion, it can occur with steroid treatment alone. Awareness of the condition is critical as prophylactic medication can be given to prevent the potentially deadly effects of tumour cell lysis.

TLS occurs from the breakdown of the tumour cells and the subsequent release of chemicals from the cell. It leads to a high potassium and high phosphate level in the presence of a low calcium. It should be suspected in any patient presenting with an acute kidney injury in the presence of a high phosphate and high uric acid level.

Prevention

- IV fluids
- patients at higher risk should receive either allopurinol or rasburicase
- rasburicase
 - a recombinant version of urate oxidase, an enzyme that metabolizes uric acid to allantoin. Allantoin is much more water-soluble than uric acid and is, therefore, more easily excreted by the kidneys
 - generally preferred now for patients at a higher risk of developing TLS
- allopurinol
 - generally used for patients in lower-risk groups
- rasburicase and allopurinol should not be given together in the management of tumour lysis syndrome as this reduces the effect of rasburicase

From 2004 TLS has been graded using the Cairo-Bishop scoring system -

Laboratory tumor lysis syndrome: abnormality in two or more of the following, occurring within three days before or seven days after chemotherapy.

- uric acid > 475 $\mu\text{mol/l}$ or 25% increase

- potassium > 6 mmol/l or 25% increase
- phosphate > 1.125mmol/l or 25% increase
- calcium < 1.75mmol/l or 25% decrease

Clinical tumor lysis syndrome: laboratory tumour lysis syndrome plus one or more of the following:

- increased serum creatinine (1.5 times upper limit of normal)
- cardiac arrhythmia or sudden death
- seizure



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Next question >

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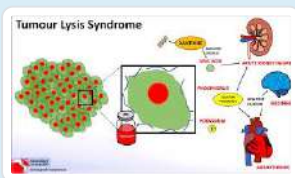


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[Tumour Lysis Syndrome](#)

Oncology for Medical Students - YouTube

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[Tumour Lysis Syndrome in 3 Minutes](#)

Townsend Teaching - YouTube

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A previously healthy 68-year-old male patient is referred by his GP to the general medical clinic. He has mixed symptoms of pain in multiple areas, including his upper arm, neck and legs. This has worsened over a period of months and seems not to have been helped with multiple analgesics, including paracetamol, codeine phosphate and ibuprofen. In this time the patient has also become increasingly short of breath.

A full work up is undertaken and the results are shown -

Hb	9.4 g/dl
Platelets	$174 \times 10^9/l$
WBC	$8.4 \times 10^9/l$

Na ⁺	136 mmol/l
K ⁺	4.7 mmol/l
Urea	8.4 mmol/l
Creatinine	125 μ mol/l
Corrected calcium	2.9mmol/l
Albumin	34g/L

Kappa light chains detected
Lambda light chains absent

IgG elevated
IgA normal
IgM normal

Urine Bence Jones proteins detected

Skeletal survey multiple osteolytic lesions seen throughout axial skeleton including on the right humerus, thoracic spine and both femurs.

Given the presumed diagnosis, what tests are most relevant for staging of the condition?

☐ Calcium, x-rays and creatinine ×

☐ Free light chain level ×

<input type="radio"/>	Renal function	×
<input type="radio"/>	B2-microglobulin and albumin	×
<input type="radio"/>	Haemaglobin and albumin	×

Submit answer

Reference ranges ▾

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Lambda light chains absent
IgG elevated
IgA normal
IgM normal

Urine Bence Jones proteins detected
Skeletal survey multiple osteolytic lesions seen throughout axial skeleton including on the right humerus, thoracic spine and both femurs.

Given the presumed diagnosis, what tests are most relevant for staging of the condition?

Calcium, x-rays and creatinine	12%
Free light chain level	10%

Renal function	2%
B2-microglobulin and albumin	75%
Haemaglobin and albumin	1%

The diagnosis here is multiple myeloma. Myeloma is a plasma cell dyscrasia that is more common in men than women. It is most common in elderly populations. The affects of myeloma can easily be remembered by the tetrad of high calcium (c), renal disease (r), anaemia (a) and bone pain (b) (crab). The original staging system was known as the Durie-Salmon Staging system which was developed in 1975. It is still commonly used as a supplementary measure but it's role in staging has been replaced by the International Staging System (ISS) that was implemented by the International Myeloma Working Group in 2005.

Discuss (5)

Improve

Next question >

Myeloma: prognosis ★

B2-microglobulin is a useful marker of prognosis - raised levels imply poor prognosis. Low levels of albumin are also associated with a poor prognosis

International prognostic index

Stage	Criteria	Median survival (months)
I	B2 microglobulin < 3.5 mg/l Albumin > 35 g/l	62
II	Not I or III	45
III	B2 microglobulin > 5.5 mg/l	29

Next question >

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Links

British Committee for Standards in Haematology

 1  3

[2014 myeloma guidelines](#)

Cancer.net

 2  1

[Multiple Myeloma: Stages](#)

[Suggest link](#)


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Media



[Multiple Myeloma Mnemonic...the story of the plasma cell](#)



Medicosis Perfectionalis - YouTube

 1  0



[Multiple Myeloma](#)

CRASH! Medical Review - YouTube

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Multiple Myeloma

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What is multiple myeloma?

Khan Academy - YouTube

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Multiple Myeloma

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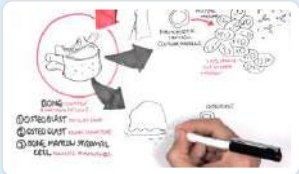
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Multiple Myeloma - Diagnosis and Treatment

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Multiple Myeloma

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A 70 year-old woman presents with severe back pain which has been worsening over the last month. Prior to this she has never suffered from back pain. She has been lethargic, and her husband notes some intermittent confusion. A systemic enquiry reveals long standing exertional breathlessness, and constipation. She has no other bowel or bladder disturbance.

Her background includes chronic obstructive pulmonary disease, which is managed by her GP. She gave up smoking two years ago. Her well woman check up 12 months ago was entirely normal, aside from a slightly raised cholesterol which is being management with diet.

On examination, she has a normal gait. There is some mild tenderness over L3/L4 vertebra with no lower limb neurological deficit. Cardiorespiratory examination reveals an ejection systolic murmur, with a normal second heart sound.

Hb	90 g/l	Na ⁺	135 mmol/l	Bilirubin	5 µmol/l
Platelets	200 * 10 ⁹ /l	K ⁺	5.5 mmol/l	ALP	101 u/l
WBC	10 * 10 ⁹ /l	Urea	15 mmol/l	ALT	40 u/l
Neuts	8 * 10 ⁹ /l	Creatinine	230 µmol/l	corrected calcium	2.7 u/l
ESR	40 mm/hr				

What is the most likely diagnosis?

- ☐ Multiple myeloma ×
- ☐ Monoclonal gammopathy of undetermined significance ×
- ☐ Non-Hodgkin's, lymphoma ×
- ☐ Paget's disease ×
- ☐ Renal cell carcinoma with spinal metastases ×

Submit answer

Reference ranges 

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Neuts	8 * 10 ⁹ /l	Creatinine	230 µmol/l	corrected calcium	2.7 u/l
ESR	40 mm/hr				

What is the most likely diagnosis?

Multiple myeloma	93%
Monoclonal gammopathy of undetermined significance	3%
Non-Hodgkin's, lymphoma	1%
Paget's disease	2%
Renal cell carcinoma with spinal metastases	2%




Multiple myeloma is malignant proliferation of plasma cells, producing a monoclonal protein detected in blood and/or urine; this causes organ or tissue damage. The median age of presentation is 70 years old.

Presenting clinical features include symptoms of:

- Impaired renal function- from light chain deposition from plasma cells, other causes include amyloid deposition, dehydration, hypercalcaemia, hyperviscosity, and nephrotoxic drugs

- Anaemia
- Hypercalcaemia- myeloma cells cause an increased production of osteoclast activating factors and cytokines that inhibit osteoblast differentiation
- Recurrent infections- decreased humoral immunity
- Hyperviscosity symptoms (headaches, epistaxis, blurred vision, and confusion)- high paraprotein levels
- Bone pain

Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic condition thought to precede multiple myeloma.

		 Discuss (6)	Improve
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Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
 - much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
 - this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding

- bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



123



Next question >

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Links

Clinical Knowledge Summaries

10 10

[Haematological cancers - recognition and referral](#)

NICE

12 6

[2016 myeloma guidelines](#)

Media



Multiple Myeloma - Diagnosis and Treatment

Medicosis Perfectionalis - YouTube

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Multiple Myeloma

Medicosis Perfectionalis - YouTube

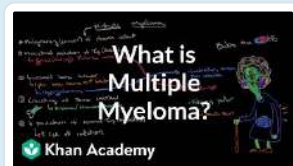
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Multiple Myeloma Mnemonic...the story of the plasma cell

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Score: **16.7%**

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Matthew is an 18-year-old man presenting with diarrhoea. The diarrhoea has been ongoing for the past 7 days and his stool is described as a type 6-7 stool on the Bristol stool charts. He did not note any blood or mucous accompanying his diarrhoea. There is accompanying crampy abdominal pains and he noted a fever of 38.2°C yesterday. He did not note any accompanying weight loss but has been feeling tired over this period.

The abdominal examination was unremarkable. He is not sexually active at present.

He has been hospitalized approximately 5-6 times in the last 3 years with recurrent infections. From his previous medical notes, his last admission related to a chest infection. He had a dry cough and shortness of breath during this time. Oxygen saturation measured on admission was 96% but quickly decreased to 89% on exertion with bilateral opacification noted on chest X-rays.

Stool cultures had been taken and on Ziehl-Neelsen staining, red oocysts are visible within the stool culture. Blood tests taken reveals:

Hb	150 g/L	Male: (135-180) Female: (115 - 160)
Platelets	250 * 10 ⁹ /L	(150 - 400)
WBC	4.5 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	1.1 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	2.5 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.6 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.3 * 10 ⁹ /L	(0.0 - 0.4)

Immunoglobulin studies were carried out and this revealed reduced levels of IgG and IgA but IgM levels were normal.

What is the most likely unifying diagnosis for his symptoms?

- ☐ Brunton's agammaglobulinemia ×
- ☐ Chediak-Higashi syndrome ×
- ☐ Selective IgA deficiency ×
- ☐ Hyper IgM syndrome ×

Submit answer

Reference ranges ▾

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Matthew is an 18-year-old man presenting with diarrhoea. The diarrhoea has been ongoing for the past 7 days and his stool is described as a type 6-7 stool on the Bristol stool charts. He did not note any blood or mucous accompanying his diarrhoea. There is accompanying crampy abdominal pains and he noted a fever of 38.2°C yesterday. He did not note any accompanying weight loss but has been feeling tired over this period.

The abdominal examination was unremarkable. He is not sexually active at present.

He has been hospitalized approximately 5-6 times in the last 3 years with recurrent infections. From his previous medical notes, his last admission related to a chest infection. He had a dry cough and shortness of breath during this time. Oxygen saturation measured on admission was 96% but quickly decreased to 89% on exertion with bilateral opacification noted on chest X-rays.

Stool cultures had been taken and on Ziehl-Neelsen staining, red oocysts are visible within the stool culture. Blood tests taken reveals:

Hb	150 g/L	Male: (135-180) Female: (115 - 160)
Platelets	250 * 10 ⁹ /L	(150 - 400)
WBC	4.5 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	1.1 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	2.5 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.6 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.3 * 10 ⁹ /L	(0.0 - 0.4)

Immunoglobulin studies were carried out and this revealed reduced levels of IgG and IgA but IgM levels were normal.

What is the most likely unifying diagnosis for his symptoms?

Brunton's agammaglobulinemia	15%
Chediak-Higashi syndrome	13%
Selective IgA deficiency	16%
Hyper IgM syndrome	36%

Hyper IgM syndrome characteristically presents with infections e.g. *Pneumocystis pneumonia*, hepatitis, diarrhoea

Important for me [Less important](#)

Hyper IgM syndrome is a rare X-linked inherited immunodeficiency that presents with multiple infections throughout their life and typically presents in infancy. It is common to see opportunistic infections as described above as cryptosporidiosis and *Pneumocystis jirovecii* pneumonia.

Definitive testing requires flow cytometry to identify the lack of expression of CD40 on T-cells or molecular genetic testing to identify a pathogenic variant on the CD40LG gene. However, findings of neutropenia and reduced IgG and IgA with normal or elevated IgM levels in patients presenting with recurrent, chronic infection highly suggests this diagnosis.

Chediak-Higashi syndrome presents with recurrent infections but this tends to be caused by more common pathogens with recurrent *Staph aureus* being the most common. It is also accompanied by other findings including albinism, photophobia and peripheral neuropathy during teenage years.

Selective IgA deficiency patients tend to be asymptomatic. However, patients can present with recurrent sinopulmonary infections and gastrointestinal infections. It is unlikely in this case due to low IgG levels as selective IgA deficiency will typically have normal IgG levels.

Brunton's agammaglobulinemia will also present with recurrent bacterial infections but investigations will reveal a generalized reduction in all immunoglobulin levels. Definitive tests include genetic testing for mutations within the BTK gene.

Wiskott-Aldrich syndrome typically presents with symptoms bruising and petechiae with eczema during the 1st month of life. Investigations will show thrombocytopenia and immunoglobulin tests will show reduced IgM but elevated IgA and IgE with normal IgG levels. Note that these patients are at increased risk of autoimmune conditions and haematology malignancy.



Discuss (4)

Improve

[Next question >](#)

Primary immunodeficiency ★

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
<u>Chronic granulomatous disease</u>	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. <i>Staphylococcus aureus</i> and fungi (e.g. <i>Aspergillus</i>) Negative nitroblue-tetrazolium test Abnormal dihydrorhodamine flow cytometry test
<u>Chediak-Higashi syndrome</u>	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen Giant granules in neutrophils and platelets
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen Absence of neutrophils/pus at sites of infection

B-cell disorders

Disorder	Underlying defect	Notes
<u>Common variable immunodeficiency</u>	Many varying causes	Low antibody levels, specifically in immunoglobulin (Ig) types IgG, IgM and IgA. Recurrent chest infections. May also predispose to autoimmune disorders and lymphoma
Bruton's (x-linked) congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen Absence of B-cells with reduced immunoglobulins of all classes
<u>Selective immunoglobulin A deficiency</u>	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and respiratory infections Associated with coeliac disease and may cause false negative coeliac antibody screen

Disorder	Underlying defect	Notes
		Severe reactions to blood transfusions may occur (anti-IgA antibodies → anaphylaxis)

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4th pharyngeal pouches	Common features include congenital heart disease (e.g. tetralogy of Fallot), learning difficulties, hypocalcaemia, recurrent viral/fungal diseases, cleft palate

Combined B- and T-cell disorders

Disorder	Underlying defect	Notes
Severe combined immunodeficiency	Many varying causes. Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. Other causes include adenosine deaminase deficiency	Recurrent infections due to viruses, bacteria and fungi. Reduced T-cell receptor excision circles Stem cell transplantation may be successful
Ataxic telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia (spider angiomas), recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopaenia. Low IgM levels Increased risk of autoimmune disorders and malignancy

Disorder	Underlying defect	Notes
Hyper IgM Syndromes	Mutations in the CD40 gene	Infection/ <i>Pneumocystis</i> pneumonia, hepatitis, diarrhoea

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Textbooks

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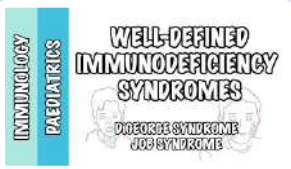
Media



[X linked agammaglobulinemia \(Bruton agammaglobulinemia\)](#)



Osmosis - YouTube

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[Well defined genetic immunodeficiency - DiGeorge Syndrome and Job Syndrome](#)

Armando Hasudungan - YouTube

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Leukocyte adhesion deficiency

Osmosis - YouTube

👍 4 👎 1



Selective immunoglobulin A deficiency

Osmosis - YouTube

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Primary antibody deficiency - Common Variable Immunodeficiency (CVID) , X-linked agammaglobulinemia

Armando Hasudungan - YouTube

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Digeorge syndrome (22q11.2 deletion syndrome)

Osmosis - YouTube

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A 54-year-old woman presents to the emergency department. She has noticed a sore throat over the last 24 hours and checked her temperature and found it to be 38.2°C. Her other observations are all normal. She has had no other symptoms and specifically denies coughing, chest pain, dysuria and diarrhoea. She is currently undergoing chemotherapy for breast cancer having last had treatment six days ago. What is the most appropriate treatment?

- ☐ Confirm neutropenia before treatment

×
- ☐ IV co-amoxiclav and oral clarithromycin

×
- ☐ Oral metronidazole

×
- ☐ IV piperacillin with tazobactam

×
- ☐ IV gentamicin

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Submit answer

Reference ranges ▾

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Question 27 of 89



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Confirm neutropenia before treatment

21%

IV co-amoxiclav and oral clarithromycin

1%

Oral metronidazole

1%

IV piperacillin with tazobactam

77%

IV gentamicin

1%

Piperacillin with tazobactam (Tazocin) is the empirical antibiotic of choice for neutropenic sepsis

Important for me Less important

The correct answer is IV piperacillin with tazobactam. This is a patient who is likely to have a low neutrophil count as she has recently had chemotherapy. Such patients should be treated as neutropenic sepsis if there is a temperature above 38°C or any other sign of sepsis, and need immediate IV piperacillin with tazobactam. Some units use vancomycin as well at this point. This should be given before confirming the neutropenia as that would cause an unnecessary delay. IV gentamicin would be generally used for pyelonephritis, whilst IV co-amoxiclav and oral clarithromycin would be used for a severe community acquired pneumonia.

Source:

'Neutropenic sepsis: prevention and management in people with cancer.' NICE guideline [CG151]. The National Institute for Health and Care Excellence, September 2012.



Discuss (2)

Improve

Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



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Next question >

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Links

NICE

👍 3 👎 1

[2012 Neutropenic sepsis guidelines](#)

Christies

👍 2 👎 4

[2013 Neutropenic sepsis guidelines](#)

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Media



[Febrile Neutropenia](#)

Townsend Teaching - YouTube

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[What is febrile neutropaenia \(neutropenia\)? - neutrophil function, pathophysiology, treatment](#)

Armando Hasudungan - YouTube

👍 2 👎 1



[Neutropenic sepsis](#)

Oncology for Medical Students - YouTube

👍 5 👎 3

Score: **16.7%**

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A 62-year-old man had a routine set of blood tests performed by his General Practitioner. These demonstrated an erythrocytosis (Packed Cell Volume 0.56) but no other abnormality. Further questioning by the GP found that the patient had no symptoms of hyperviscosity, was a non-smoker with no symptoms of daytime somnolence and took no regular medications. Past medical history included only a left knee hemiarthroplasty performed due to osteoarthritis.

Two weeks after the initial blood test, the patient's bloods were repeated and showed the persistence of the erythrocytosis. A referral to haematology clinic was made for further investigation. Details of further investigations arranged through haematology clinic are listed below.

Haemoglobin	188 g / L
White cell count	$6.7 \times 10^9/\text{l}$
Neutrophils	$3.2 \times 10^9/\text{l}$
Lymphocytes	$2.1 \times 10^9/\text{l}$
Monocytes	$0.8 \times 10^9/\text{l}$
Eosinophils	$0.3 \times 10^9/\text{l}$
Basophils	$0.3 \times 10^9/\text{l}$
Platelets	$202 \times 10^9/\text{l}$
Packed cell volume	0.59
Urea	4.5 mmol / L
Creatinine	97 micromol / L
Sodium	140 mmol / L
Potassium	3.9 mmol / L
eGFR	85 ml / min
Ferritin	80 ng / ml
Albumin	38 g / L
Alkaline phosphatase	89 U / L
ALT	25 U / L
Bilirubin	20 micromol / L
JAK 2 V617F mutation	Negative
Serum erythropoietin	0 U / L (reference 0-19)

Blood film: no abnormality detected; no features of myeloproliferative disease

Abdominal ultrasound: liver, hepatic duct system and gallbladder unremarkable; mild-moderate splenomegaly; kidneys and renal tract unremarkable

What is the most appropriate next investigation?

- ☐ JAK2 exon 12 mutation testing
- ☐ Bone marrow aspiration and trephine biopsy
- ☐ Measurement of red cell mass
- ☐ CT brain
- ☐ Erythropoietin receptor gene analysis

Submit answer

Reference ranges ▾

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Blood film: no abnormality detected; no features of myeloproliferative disease

Abdominal ultrasound: liver, hepatic duct system and gallbladder unremarkable; mild-moderate splenomegaly; kidneys and renal tract unremarkable

What is the most appropriate next investigation?

JAK2 exon 12 mutation testing	42%
Bone marrow aspiration and trephine biopsy	21%
Measurement of red cell mass	25%
CT brain	1%
Erythropoietin receptor gene analysis	12%

Erythrocytosis is defined as a haemoglobin > 18.5 g / dL or PCV > 0.52 (male) / 0.48 (female). Patients with a persistent erythrocytosis without a clear cause (i.e. chronic hypoxia or drug causes) should be referred to haematology for further investigation. An urgent referral should be made if symptoms of hyperviscosity or polycythaemia (raised PCV, white cells and platelets) are present.

More than 95 % of individuals with polycythaemia vera test positive for the JAK 2 V617F mutation. Other baseline investigations include a blood film to exclude myeloproliferative disease, renal and liver profiles and serum ferritin (as iron deficiency can mask the degree of erythrocytosis). Abdominal ultrasound is performed in patients with high suspicion for polycythaemia vera as this condition is associated with radiographical splenomegaly in two-thirds of cases.

A low serum erythropoietin is suggestive of primary bone marrow disease even in the absence of JAK 2 mutation and should prompt testing for the rarer exon 12 mutation of JAK 2. This test should be performed before the more invasive bone marrow biopsy.

Raised serum erythropoietin should prompt investigation for an exogenous source, for example, CT brain to look for a cerebellar haemangioma or meningioma.

In patients without a JAK 2 mutation and a normal erythropoietin level then measurement of red cell mass will distinguish between a true erythrocytosis and an apparent erythrocytosis (normal red cell mass but reduced plasma volume).

Rare congenital mutations in the erythropoietin receptor can also cause a primary erythrocytosis. Keohane C, McMullin M, Harrison C. The diagnosis and management of erythrocytosis. BMJ 2013;347:f6667.

Polycythaemia vera: features ★

Polycythaemia vera (previously called polycythaemia rubra vera) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with polycythaemia vera and this has resulted in significant changes to the diagnostic criteria. The incidence of polycythaemia vera peaks in the sixth decade.

Features

- pruritus, typically after a hot bath
- splenomegaly
- hypertension
- hyperviscosity
 - arterial thrombosis
 - venous thrombosis
- haemorrhage (secondary to abnormal platelet function)
- low ESR

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed

- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:

- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphatase

The diagnostic criteria for polycythaemia vera have recently been updated by the BCSH. This replaces the previous polycythaemia vera Study Group criteria.

JAK2-positive polycythaemia vera - diagnosis requires both criteria to be present

Criteria	Notes
A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

Criteria	Notes
A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count $>450 \times 10^9/l$)
B2	Neutrophil leucocytosis (neutrophil count $> 10 \times 10^9/l$ in non-smokers; $> 12.5 \times 10^9/l$ in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin



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Links

Clinical Knowledge Summaries

👍 1 🗑️ 3

[Polycythaemia guidelines](#)

British Committee for Standards in Haematology

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[2005 polycythaemia guidelines](#)

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Media



[Polycythemia Vera](#)

Medicosis Perfectionalis - YouTube

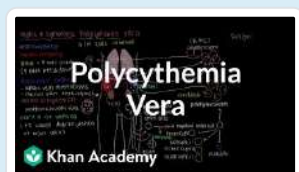
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[Polycythemia vera](#)

Osmosis - YouTube

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[What is polycythemia vera?](#)

Khan Academy - YouTube

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Polycythemia: Clinical Features, Management and Mnemonics

Townsend Teaching - YouTube

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A 78-year-old man presents to the acute medical unit with a 3-day history of lower limb weakness. He has a 6-month history of progressive back pain. He denies any bowel or bladder dysfunction, and saddle anaesthesia.

Blood results are as follows:

Hb	110 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$182 \times 10^9/L$	(150 - 400)
WBC	$6.8 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	134 mmol/L	(135 - 145)
K ⁺	5.1 mmol/L	(3.5 - 5.0)
Urea	16.2 mmol/L	(2.0 - 7.0)
Creatinine	288 μ mol/L	(55 - 120)

Paraprotein	No paraprotein detected	
Kappa free light chains	12,450 mg/L	(3.3 - 19.4)
Lambda free light chains	125 mg/L	(5.7 - 26.3)
Kappa to Lambda ratio	99.6	(0.26 - 1.65)

An MRI spine confirms cauda equina syndrome due to a large paravertebral soft tissue mass. In addition, there is widespread abnormal marrow involvement throughout the spine.

What is the most likely diagnosis?

- ☐ High grade B cell lymphoma
- ☐ Multiple myeloma
- ☐ Prostate carcinoma
- ☐ Solitary bone plasmacytoma
- ☐ Solitary extra medullary plasmacytoma

Submit answer

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An MRI spine confirms cauda equina syndrome due to a large paravertebral soft tissue mass. In addition, there is widespread abnormal marrow involvement throughout the spine.

What is the most likely diagnosis?

High grade B cell lymphoma	6%
Multiple myeloma	60%
Prostate carcinoma	3%
Solitary bone plasmacytoma	12%
Solitary extra medullary plasmacytoma	19%

In approximately 1-2% of myeloma cases, the myeloma cells produce very low amounts of paraprotein, which can only be detected using the serum free light chain test. This is called oligosecretory myeloma

Important for me Less important



The diagnosis is most certainly **multiple myeloma** due to evidence of a monoclonal plasma cell population (markedly raised kappa to lambda ratio) and myelomatous end-organ dysfunction (e.g. anaemia, renal dysfunction and diffuse bone involvement). Although the paraprotein is negative, in approximately 1-2% of myeloma cases, the myeloma cells produce very low amounts of paraprotein, which can only be detected using the highly sensitive serum free light chain test.

Light chains are secreted by B-cells and plasma cells. Individual B- or plasma cells possess either kappa or lambda light chains, but never both together. Interpretation of serum free light chains (sFLC) can be confusing. It is important to remember that it is the ratio that is the most important aspect of the analysis. Several diseases can give rise to increased absolute levels of sFLC. For example due to decreased excretion as seen in renal failure, or due to increased production (e.g. infections, or inflammatory conditions). These 'reactive' causes will result in a broadly similar increase in both kappa and lambda light chains thereby maintaining a normal ratio. However, in monoclonal conditions, the B-cell or plasma cell clone will be either lambda or kappa light chain restricted subsequently resulting in an abnormal ratio.

The large soft tissue mass likely represents an extramedullary plasmacytoma. However, the diagnosis of a **solitary extramedullary plasmacytoma** is excluded given that the patient has myelomatous end-organ dysfunction and involvement of the axial skeleton.

Similarly, a **solitary bone plasmacytoma** is excluded due to the absence of a bone plasmacytoma and the presence of myelomatous end-organ dysfunction.

Although lymphomas can present with soft tissue masses and produce light chains, the clinical features (e.g. anaemia and renal impairment) are more in keeping with myeloma, making a **high-grade B cell lymphoma** less likely.

Prostate carcinoma classically presents with sclerotic bone metastases, and would not cause an abnormal serum free light chain ratio.



Discuss (2)

Improve

Next question >

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia
 - primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
 - much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
 - this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



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Textbooks

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Links

Clinical Knowledge Summaries

10 10

[Haematological cancers - recognition and referral](#)

NICE

12 6

[2016 myeloma guidelines](#)

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Media



[Multiple Myeloma - Diagnosis and Treatment](#)

Medicosis Perfectionalis - YouTube

6 0



[Multiple Myeloma](#)

Medicosis Perfectionalis - YouTube

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Multiple Myeloma Mnemonic...the story of the plasma cell

Medicosis Perfectionalis - YouTube

👍 5 🗨️ 1



What is multiple myeloma?

Khan Academy - YouTube

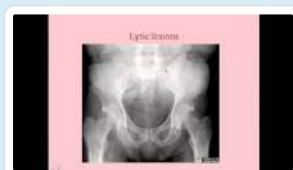
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Multiple Myeloma

Townsend Teaching - YouTube

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Multiple Myeloma

CRASH! Medical Review - YouTube

👍 0 🗨️ 1



Multiple Myeloma

Armando Hasudungan - YouTube

👍 1 🗨️ 3

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A 72-year-old man attends the emergency department with a headache and blurred vision which has progressively worsened over the past 2 weeks. On examination, his observations are within normal limits, and he has no focal neurology. On fundoscopy, there is bilateral retinal vein dilation and tortuosity with visible retinal haemorrhages.

Blood results are as follows:

Hb	90 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$110 \times 10^9/L$	(150 - 400)
WBC	$4.8 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	10.8 mmol/L	(2.0 - 7.0)
Creatinine	184 $\mu\text{mol/L}$	(55 - 120)
CRP	4 mg/L	(< 5)
Plasma viscosity	4.2mPas	(1.50 -1.72)

IgG	1.2 g/L	(6-16)
IgM	42 g/L	(0.4 - 2.5)
IgA	0.2 g/L	(0.8 - 3.0)

Given the likely diagnosis, what treatment is urgently indicated?

- ☐ Chemotherapy ×
- ☐ Ibrutinib ×
- ☐ Plasma exchange ×
- ☐ Red cell transfusion ×
- ☐ Steroids ×

Submit answer

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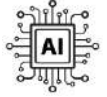
Hb	90 g/L	Male: (135-180) Female: (115 - 160)
Platelets	110 * 10 ⁹ /L	(150 - 400)
WBC	4.8 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
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Urea	10.8 mmol/L	(2.0 - 7.0)
Creatinine	184 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Plasma viscosity	4.2mPas	(1.50 -1.72)

IgG	1.2 g/L	(6-16)
IgM	42 g/L	(0.4 - 2.5)
IgA	0.2 g/L	(0.8 - 3.0)

Given the likely diagnosis, what treatment is urgently indicated?

Chemotherapy	14%
Ibrutinib	8%
Plasma exchange	68%
Red cell transfusion	1%
Steroids	9%

Patients with Waldenstrom's macroglobulinaemia often present with issues secondary to hyperviscosity



The patient has clinical features of hyperviscosity (e.g. headache, blurred vision, and renal impairment). This is confirmed biochemically with the raised plasma viscosity. The fundoscopic appearances (bilateral retinal vein dilation and tortuosity with retinal haemorrhages) are also classic for hyperviscosity within the retinal vasculature.

The markedly raised IgM level is suggestive of Waldenstrom's macroglobulinaemia.

The presence of anaemia and thrombocytopenia are most likely due to bone marrow infiltration. However alternative causes should also be considered (e.g. autoimmune haemolytic anaemia, and immune thrombocytopenia).

Plasma exchange is correct. Hyperviscosity is a haematological emergency and the patient thus needs emergency plasma exchange. Plasma exchange is an extra-corporeal technique able to remove macromolecules (e.g. IgM) from blood.

Chemotherapy is incorrect. Although the patient will most certainly need chemotherapy to treat their underlying disorder, the first priority is to treat the hyperviscosity by reducing the IgM level with plasma exchange.

Ibrutinib is incorrect. Ibrutinib is a type of tyrosine kinase inhibitor (TKI) that is highly efficacious in a variety of haematological malignancies. It is less toxic compared to traditional chemotherapies and is therefore often used as a first-line agent in frail elderly patients. It can also be used in Waldenstrom's macroglobulinaemia however at the current time the priority is for plasma exchange.

Red cell transfusion is incorrect. Although the patient is anaemic, they most certainly should not receive a red cell transfusion at the current time as this could worsen the hyperviscosity.

Steroids is incorrect. Steroids are often used as chemotherapy adjuncts to treat Waldenstrom's macroglobulinaemia, however at the current time the priority is for plasma exchange.



Discuss (3)

Improve

Next question >

Waldenstrom's macroglobulinaemia ★

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
 - the pentameric configuration of IgM increases serum viscosity
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Investigations

- monoclonal IgM paraproteinaemia
- bone marrow biopsy is diagnostic
 - infiltration of the bone marrow with lymphoplasmacytoid lymphoma cells

Management

- typically rituximab-based combination chemotherapy



123



Next question >

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[Waldenstrom's macroglobulinaemia](#)

Medicosis Perfectionalis - YouTube

👍 6 👎 0



Waldenstrom's macroglobulinaemia

Osmosis - YouTube

👍 5 👎 0



What is Waldenstrom's macroglobulinaemia

Khan Academy Medicine - YouTube

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Score: **16.7%**

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A 35-year-old woman who was diagnosed with hereditary angioedema is about to undergo an elective meniscal repair for her left knee. She has been well otherwise with no recent changes to her health or medications. Which is the drug of choice for prophylaxis for her hereditary angioedema prior to her procedure?

- | | | |
|-----------------------|-----------------|---|
| <input type="radio"/> | Prednisolone | × |
| <input type="radio"/> | Hydrocortisone | × |
| <input type="radio"/> | Conestat alfa | × |
| <input type="radio"/> | Tranexamic acid | × |
| <input type="radio"/> | Icatibant | × |

Submit answer

Reference ranges ▾

Score: 16.7%

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Question 31 of 89



A 35-year-old woman who was diagnosed with hereditary angioedema is about to undergo an elective meniscal repair for her left knee. She has been well otherwise with no recent changes to her health or medications. Which is the drug of choice for prophylaxis for her hereditary angioedema prior to her procedure?

Prednisolone	11%
Hydrocortisone	11%
Conestat alfa	28%
Tranexamic acid	16%
Icatibant	33%

The best answer here is tranexamic acid.

In hereditary angioedema, the relevant medications can be used as follows:

A C1-esterase inhibitor can be used for short-term prophylaxis before procedures or to terminate acute attacks of hereditary angioedema. Conestat alfa and icatibant are licensed for the treatment of acute attacks of hereditary angioedema in adults with C1-esterase inhibitor deficiency.

Tranexamic acid and danazol are used for short-term and long-term prophylaxis.

There is no role of glucocorticoids in this case.



 Discuss (7)
  Improve

Next question >

Hereditary angioedema ★

Hereditary angioedema (HAE) is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH, C1 esterase inhibitor) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

Investigation

- C1-INH level is low during an attack

- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

Symptoms

- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

Management

- acute
 - HAE does not respond to adrenaline, antihistamines, or glucocorticoids
 - IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help



123



Next question >

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Links

Patient.info



1



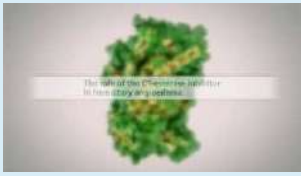
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[Hereditary angioedema review](#)

[Suggest link](#)

[Report broken link](#)

Media



The Role of the C1-Esterase Inhibitor in HAE

Individual - YouTube

👍 3 👎 0

[Report broken media](#)

Score: **16.1%**

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Question 32 of 89



A 65-year-old woman presents to the emergency department with a painful leg. She had noticed that her calf started to become tender when she was getting dressed in the morning and found it to be swollen. She was concerned and called her GP surgery who gave her an emergency appointment. She was seen by her GP earlier in the day who suspected a deep vein thrombosis and advise her to attend her local emergency department.

She has a past medical history of breast cancer which was operated on three months ago with a wide local excision, and she has been told that the operation was successful in removing the cancer. Her observations are stable. On examination, she has a swollen left calf which is mildly tender without erythema. A D-dimer sent by the emergency department team was positive but all other blood tests are normal. She undergoes a doppler ultrasound scan which shows no thrombus. How should she be further managed?

- ☐ Start warfarin ×
- ☐ Repeat ultrasound scan within 6-8 days ×
- ☐ CT pulmonary angiogram ×
- ☐ Start treatment dose low-molecular weight heparin ×
- ☐ Repeat D-dimer ×

Submit answer

Reference ranges 

Score: **16.1%**

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A 65-year-old woman presents to the emergency department with a painful leg. She had noticed that her calf started to become tender when she was getting dressed in the morning and found it to be swollen. She was concerned and called her GP surgery who gave her an emergency appointment. She was seen by her GP earlier in the day who suspected a deep vein thrombosis and advise her to attend her local emergency department.

She has a past medical history of breast cancer which was operated on three months ago with a wide local excision, and she has been told that the operation was successful in removing the cancer. Her observations are stable. On examination, she has a swollen left calf which is mildly tender without erythema. A D-dimer sent by the emergency department team was positive but all other blood tests are normal. She undergoes a doppler ultrasound scan which shows no thrombus. How should she be further managed?

Start warfarin	2%
Repeat ultrasound scan within 6-8 days	67%
CT pulmonary angiogram	10%
Start treatment dose low-molecular weight heparin	20%
Repeat D-dimer	2%

The correct answer is to repeat the ultrasound scan within 6-8 days. This is a patient with a major risk factor for deep vein thrombosis (DVT) and pulmonary embolus (PE) who presents with typical features of a DVT; unilateral tender and swollen calf. She would likely have a Well's score at 2 and be considered at high risk.

Since the ultrasound is negative, a repeat ultrasound is advised, and there as of yet no indications to start treatment with either warfarin or heparin. In patients with cancer warfarin is not recommended as treatment for DVT or PE. A CT pulmonary angiogram is not indicated as there are no symptoms or signs suggestive of a pulmonary embolus. Repeating the D-dimer is unlikely to give any additional information.

'Venous thromboembolic diseases: diagnosis, management and thrombophilia testing' Clinical guideline [CG144]. The National Institute for Health and Care Excellence, June 2012.

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)
 - interim therapeutic anticoagulation used to mean giving low-molecular weight heparin
 - NICE updated their guidance in 2020. They now recommend using an anticoagulant that can be continued if the result is positive.
 - this means normally a direct oral anticoagulant (DOAC) such as apixaban or rivaroxaban
- if the scan is negative but the D-dimer is positive:
 - stop interim therapeutic anticoagulation
 - offer a repeat proximal leg vein ultrasound scan 6 to 8 days later

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test
 - this should be done within 4 hours. If not, interim therapeutic anticoagulation should be given until the result is available
 - if the result is negative then DVT is unlikely and alternative diagnoses should be considered
 - if the result is positive then a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if a proximal leg vein ultrasound scan cannot be carried out within 4 hours interim therapeutic anticoagulation should be administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

D-dimer tests

- NICE recommend either a point-of-care (finger prick) or laboratory-based test
- age-adjusted cut-offs should be used for patients > 50 years old



2 level DVT tests		
Feature	Points	
Active cancer (current or past), recent surgery, trauma, or childbirth	1	Score 3-5 points = DVT likely Score 0-2 points = DVT unlikely
Recent surgery, trauma, or recent plaster immobilisation of the lower extremities	1	
Recent immobilisation for 3 days or more or major surgery within 12 weeks, including general or regional anaesthesia	1	
Isolated haematuria using the detection of the three voids system	1	
Bedridden patient	1	
Swelling in both legs or both arms larger than upper arm/leg	1	
Plasma D-dimer concentration > 0.5 µg/L (symptomatic leg)	1	
Confirmed proximal venous thrombosis	1	
Previously documented DVT	1	
An alternative diagnosis is at least as likely as DVT	-2	

Management

The cornerstone of VTE management is anticoagulant therapy. This was historically done with warfarin, often preceded by heparin until the INR was stable. However, the development of DOACs, and an evidence base supporting their efficacy, has changed modern management.

Choice of anticoagulant

- the big change in the 2020 guidelines was the increased use of DOACs
- apixaban or rivaroxaban (both DOACs) should be offered first-line following the diagnosis of a DVT
 - instead of using low-molecular weight heparin (LMWH) until the diagnosis is confirmed, NICE now advocate using a DOAC once a diagnosis is suspected, with this continued if the diagnosis is confirmed
 - if neither apixaban or rivaroxaban are suitable then either LMWH followed by dabigatran or edoxaban OR LMWH followed by a vitamin K antagonist (VKA, i.e. warfarin)
- if the patient has active cancer
 - previously LMWH was recommended
 - the new guidelines now recommend using a DOAC, unless this is contraindicated
- if renal impairment is severe (e.g. $< 15/\text{min}$) then LMWH, unfractionated heparin or LMWH followed by a VKA
- if the patient has antiphospholipid syndrome (specifically 'triple positive' in the guidance) then LMWH followed by a VKA should be used

Length of anticoagulation

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer at increased risk
 - an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



123



Next question >



Textbooks

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Links

NICE

 5  0

[2020 Venous thromboembolism guidelines](#)

[Suggest link](#)

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Media



[Deep vein thrombosis](#)



Osmosis - YouTube

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[Understanding Deep Vein Thrombosis \(DVT\)](#)

Zero To Finals - YouTube

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
















[Deep Vein Thrombosis - Overview \(pathophysiology, treatment, complications\)](#)

Armando Hasudungan - YouTube

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- 50 ✖



A 44-year-old female is referred to haematology outpatients with fatigue, shortness of breath and abnormal blood results organized by her general practitioner. She has no past medical history and is on no medications. She does not smoke or drink alcohol. She works in a bakery.

Clinical examination is unremarkable.

Blood tests:

Hb	101 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$111 \times 10^9/\text{L}$	(150 - 400)
WBC	$14.2 \times 10^9/\text{L}$	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.1 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	88 $\mu\text{mol/L}$	(55 - 120)
CRP	4 mg/L	(< 5)

A blood film is organized, which demonstrates Auer rods.

What is the most likely diagnosis?

- ☐ Acute lymphocytic leukaemia ×
- ☐ Acute promyelocytic leukaemia ×
- ☐ Chronic lymphocytic leukaemia ×
- ☐ Chronic myeloid leukaemia ×
- ☐ Thrombotic thrombocytopenic purpura ×

Submit answer

Reference ranges ∨

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A 44-year-old female is referred to haematology outpatients with fatigue, shortness of breath and abnormal blood results organized by her general practitioner. She has no past medical history and is on no medications. She does not smoke or drink alcohol. She works in a bakery.

Clinical examination is unremarkable.

Blood tests:

Hb	101 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$111 \times 10^9/L$	(150 - 400)
WBC	$14.2 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.1 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	88 $\mu\text{mol/L}$	(55 - 120)
CRP	4 mg/L	(< 5)

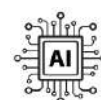
A blood film is organized, which demonstrates Auer rods.

What is the most likely diagnosis?

Acute lymphocytic leukaemia	6%
Acute promyelocytic leukaemia	79%
Chronic lymphocytic leukaemia	2%
Chronic myeloid leukaemia	11%
Thrombotic thrombocytopenic purpura	1%

Auer rods on blood film strongly suggests acute promyelocytic leukaemia

Important for me Less important




Acute promyelocytic leukaemia is the correct answer. The full blood count, in this case, demonstrates two cell lineages with cytopenias. The white cell count can be raised in this type of leukaemia but not all of the white blood cells will be functional, and she will be at higher risk of infection. The blood film is highly suggestive of acute promyelocytic leukaemia.

Acute lymphocytic leukaemia is incorrect. Auer rods are not typical of the peripheral blood film in this condition. It may show blast cells in this case or it may be normal if the cells are confined to the bone marrow.

Chronic myeloid leukaemia is incorrect. The blood film in this case would not demonstrate Auer rods but rather a significant leucocytosis consisting of the whole spectrum of mature granulocytes. Organomegaly and lymphadenopathy are common.

Chronic lymphocytic leukaemia is incorrect. This typically affects an older age range with a significant lymphocytosis. The blood film may show 'smear' cells.

Thrombotic thrombocytopenic purpura is incorrect. Clinically this is often characterized by confusion, headache, fever and bruising. It is a medical emergency. The blood film will show schistocytes.

		 Discuss (3)	Improve
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Next question >

Acute myeloid leukaemia ★

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Features are largely related to bone marrow failure:

- anaemia: pallor, lethargy, weakness
- neutropenia: whilst white cell counts may be very high, functioning neutrophil levels may be low leading to frequent infections etc
- thrombocytopenia: bleeding
- splenomegaly
- bone pain

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- Auer rods (seen with myeloperoxidase stain)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)

- M0 - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic



123



Next question >

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Links

Clinical Knowledge Summaries



7



11

[Haematological cancers - recognition and referral](#)

[Suggest link](#)

[Report broken link](#)

Media



Acute myeloid & lymphoblastic leukemia

Osmosis - YouTube



9



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[Report broken media](#)

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A 58-year-old male is referred to the haematology outpatient department with reports of widespread bruising. He does not have any significant past medical history and does not take any regular medications. He does not smoke or drink alcohol.

On examination, there are widespread ecchymoses affecting all of his limbs, abdomen and thorax.

Blood tests:

Hb	111 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$167 \times 10^9/L$	(150 - 400)
WBC	$4.2 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	88 $\mu\text{mol/L}$	(55 - 120)
CRP	4 mg/L	(< 5)
Activated partial thromboplastin time (APTT)	61 seconds	(30-40)
Prothrombin time	11 seconds	(11 - 12.5)
Factor VIII	8 IU/dl	(50-150)
Bleeding time	5 minutes	(3-10)
Lupus anticoagulant	absent	(present)

A mixing study is abnormal and further testing demonstrates the presence of factor VIII inhibitor.

What is the most likely diagnosis?

- ☐ Acquired haemophilia A ×
- ☐ Haemophilia B ×
- ☐ Hereditary haemophilia A ×
- ☐ Vitamin K deficiency ×
- ☐ Von Willebrand's disease ×

Submit answer

Reference ranges 

Score: **16.1%**

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A 58-year-old male is referred to the haematology outpatient department with reports of widespread bruising. He does not have any significant past medical history and does not take any regular medications. He does not smoke or drink alcohol.

On examination, there are widespread ecchymoses affecting all of his limbs, abdomen and thorax.

Blood tests:

Hb	111 g/L	Male: (135-180) Female: (115 - 160)
Platelets	167 * 10 ⁹ /L	(150 - 400)
WBC	4.2 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Activated partial thromboplastin time (APTT)	61 seconds	(30-40)
Prothrombin time	11 seconds	(11 - 12.5)
Factor VIII	8 IU/dl	(50-150)
Bleeding time	5 minutes	(3-10)
Lupus anticoagulant	absent	(present)

A mixing study is abnormal and further testing demonstrates the presence of factor VIII inhibitor.

What is the most likely diagnosis?

Acquired haemophilia A	73%
Haemophilia B	2%
Hereditary haemophilia A	7%
Vitamin K deficiency	1%
Von Willebrand's disease	16%

Acquired haemophilia A is diagnosed in patients without previous or familial histories of bleeding who have isolated prolongation of the activated partial thromboplastin time (aPTT), reduced FVIII levels as well as evidence of FVIII inhibitor activity

Important for me Less important

Acquired haemophilia A is the correct answer. This acquired haemophilia presents in later life without a preceding history of coagulopathy or family history. It is characterised by an isolated prolongation of the activated partial thromboplastin time (aPTT), reduced FVIII levels as well as evidence of FVIII inhibitor activity. It typically presents with bleeding into the skin or muscles and occasionally haematuria or melena. Haemarthrosis is less likely than with an inherited haemophilia. It is autoimmune disorder with the formation of antibodies that attack clotting factors. A mixing study is crucial in differentiating inherited factor deficiencies from acquired factor deficiencies. In inherited disorders that are characterized by a factor deficiency, the addition of normal plasma to blood restores the clotting parameters. In individuals with a factor inhibitor, the coagulation test remains abnormal.

Haemophilia B is incorrect. This is inherited bleeding disorder characterised by deficiency of factor IX.

Hereditary haemophilia A is incorrect. The absence of a family history, bleeding from a young age and normal mixing study, make this an unlikely diagnosis.

Vitamin K deficiency is incorrect. This will cause an abnormal PT and APTT.

Von Willebrand's disease is incorrect. This will cause an abnormal bleeding time.



Discuss (1)

Improve

Next question >

Abnormal coagulation ★

Cause	Factors affected
Heparin	Prevents activation factors 2,9,10,11
Warfarin	Affects synthesis of factors 2,7,9,10
DIC	Factors 1,2,5,8,11
Liver disease	Factors 1,2,5,7,9,10,11

Interpretation blood clotting test results

Disorder	APTT	PT	Bleeding time
Haemophilia	Increased	Normal	Normal
von Willebrand's disease	Increased	Normal	Increased
Vitamin K deficiency	Increased	Increased	Normal

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Next question >


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Media




Coagulation cascade


DirtyUSMLE - YouTube



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Coagulation cascade

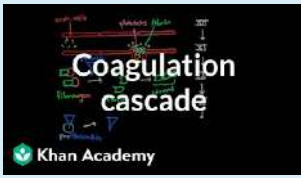
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Coagulation cascade

KhanAcademy - YouTube

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A 55-year-old woman is referred to the haematology outpatient department with unexplained eosinophilia. She has a past medical history of systemic lupus erythematosus and recurrent urinary tract infections. Her regular medications include azathioprine and nitrofurantoin.

On examination, there is a rash across the malar region that spares the nasolabial folds but is otherwise unremarkable.

Plain radiography of the chest is unremarkable.

Hb	136 g/L	Male: (135-180) Female: (115 - 160)
Platelets	189 * 10 ⁹ /L	(150 - 400)
WBC	8.2 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	5.2 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	2.0 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.8 * 10 ⁹ /L	(0.0 - 0.4)

What is the most likely explanation for her eosinophilia?

- ☐ Azathioprine ×
- ☐ Eosinophilic granulomatosis with polyangiitis ×
- ☐ Hypereosinophilic syndrome ×
- ☐ Nitrofurantoin ×
- ☐ Systemic lupus erythematosus ×

Submit answer

Reference ranges 

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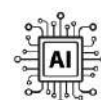
Hb	136 g/L	Male: (135-180) Female: (115 - 160)
Platelets	189 * 10 ⁹ /L	(150 - 400)
WBC	8.2 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	5.2 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	2.0 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.8 * 10 ⁹ /L	(0.0 - 0.4)

What is the most likely explanation for her eosinophilia?

Azathioprine	11%
Eosinophilic granulomatosis with polyangiitis	3%
Hypereosinophilic syndrome	15%
Nitrofurantoin	60%
Systemic lupus erythematosus	10%

Nitrofurantoin can cause eosinophilia

Important for me Less important



Nitrofurantoin is correct. This is an antibiotic used for urinary-tract infections, sometimes given as a prophylactic long-term dose to prevent recurrent infections. It is associated with eosinophilia as


a recognised side effect and is the most likely explanation in this case.

Azathioprine is incorrect. Eosinophilia is not a common side effect of this medication. Indeed, it may be used as a steroid-sparing agent in some hyper-eosinophilic syndromes. It is more likely to cause cytopenias as a side effect.

Eosinophilic granulomatosis with polyangiitis (EGPA) is incorrect. A malar rash is not typical of EGPA but rather of lupus. EGPA typically causes a vasculitic rash, which would be non-blanching and not likely to be located in the malar region. Additionally, there is no history of asthma or sinus problems, making the diagnosis unlikely. Furthermore, the eosinophil count in this disorder tends to be $> 1.5 \times 10^9/L$.

Hypereosinophilic syndrome is incorrect. This is a myeloproliferative disorder associated with persistent eosinophilia and organ damage. The eosinophil count must be at least $1.5 \times 10^9/L$ for this diagnosis to be considered.

Systemic lupus erythematosus (SLE) is incorrect. This disorder is associated with haematological abnormalities. However, active SLE is typically associated with cytopenias (anaemia, thrombocytopenia, leucopenia) rather than the converse. Eosinophilia is not typical.

		 Discuss (2)	Improve
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Next question >

Eosinophilia ★

Causes of eosinophilia may be divided into pulmonary, infective and other

Pulmonary causes

- asthma
- allergic bronchopulmonary aspergillosis
- Churg-Strauss syndrome
- Löffler's syndrome
- tropical pulmonary eosinophilia
- eosinophilic pneumonia
- hypereosinophilic syndrome

Infective causes

- schistosomiasis
- nematodes: Toxocara, Ascaris, Strongyloides
- cestodes: Echinococcus

Other causes


- drugs: sulfasalazine, nitrofurantoin
- psoriasis/eczema
- eosinophilic leukaemia (very rare)

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Next question >


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Textbooks

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Question 36 of 89



A 74-year-old patient is referred to the haematology outpatient clinic with a lump in her neck. She has no past medical history.

On examination, widespread lymphadenopathy is detectable in the cervical, inguinal and axillary regions.

Hb	121 g/L	Male: (135-180) Female: (115 - 160)
Platelets	189 * 10 ⁹ /L	(150 - 400)
WBC	95 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	2.0 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	92.7 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.1 * 10 ⁹ /L	(0.0 - 0.4)

Given the presentation, what is the most important investigation to confirm the diagnosis?

- ☐ Bone marrow aspiration ×
- ☐ Bone marrow trephine biopsy ×
- ☐ Cytogenetics ×
- ☐ Immunophenotyping ×
- ☐ Labelled white blood cell scan ×

Submit answer

Reference ranges 

Score: **16.1%**

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On examination, widespread lymphadenopathy is detectable in the cervical, inguinal and axillary regions.

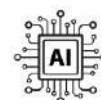
Hb	121 g/L	Male: (135-180) Female: (115 - 160)
Platelets	189 * 10 ⁹ /L	(150 - 400)
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Eosin	0.1 * 10 ⁹ /L	(0.0 - 0.4)

Given the presentation, what is the most important investigation to confirm the diagnosis?



CLL - immunophenotyping is investigation of choice

Important for me Less important



Immunophenotyping is incorrect. Immunophenotyping by flow cytometry is a method used to detect the presence or absence of white blood cell antigens. These antigens are protein structures associated with white blood cells. Specific groupings of these antigens are normally present on or within white blood cells (WBCs) and are unique to specific cell types and stages of cell maturation.


Specific patterns of antigens are present on abnormal cells seen in specific lymphomas like chronic lymphocytic leukaemia (CLL). On flow cytometry, CLL cells classically demonstrate CD5, CD19, CD23, weak monotypic surface immunoglobulin and weak or absent CD79B, CD22 and FMC7.

Bone marrow aspiration is incorrect. A bone marrow aspirate contains a liquid sample from the bone marrow for analysis. Bone marrow (BM) aspirate and trephine biopsy is not typically necessary at diagnosis but is used in cases with atypical features or to rule out differential diagnoses in the case of anaemia/thrombocytopenia.

Bone marrow trephine biopsy is incorrect. A trephine biopsy removes a small piece of bone with the marrow inside. Again, this is not required at diagnosis. Bone marrow trephine biopsies may show interstitial, nodular or diffuse infiltration if carried out.

Cytogenetics is incorrect. This may be used to inform prognosis (as a complex karyotype is associated with poor survival). However, it is not typically required at diagnosis.

Labelled white blood cell scan is incorrect. This scan is typically used to localise a site of unknown infection rather than diagnose CLL.

		 Discuss (2)	Improve
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Next question >

Chronic lymphocytic leukaemia: features and investigation ★

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%). It is the most common form of leukaemia seen in adults.

Features

- often none: may be picked up by an incidental finding of lymphocytosis
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than chronic myeloid leukaemia

Investigations

- full blood count:
 - lymphocytosis
 - anaemia: may occur either due to bone marrow replacement or autoimmune hemolytic anaemia (AIHA)
 - thrombocytopenia: may occur either due to bone marrow replacement or immune thrombocytopenia (ITP)
- blood film: smudge cells (also known as smear cells)

- immunophenotyping is the key investigation
 - most cases can be identified using a panel of antibodies specific for CD5, CD19, CD20 and CD23

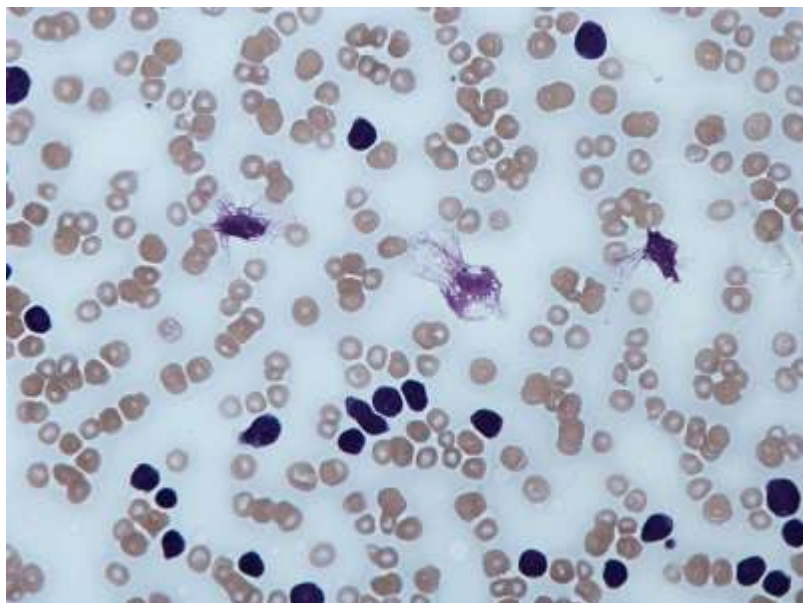


Image sourced from Wikipedia

Peripheral blood film showing smudge B cells



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

👍 5 👎 4

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

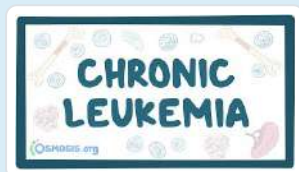
Media



Chronic Lymphocytic Leukemia (CLL) - Diagnosis & Treatment

Medicosis Perfectionalis - YouTube

👍 2 👎 0



Chronic leukemia

Osmosis - YouTube

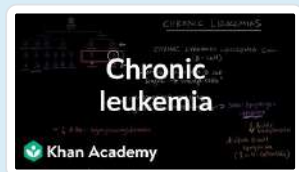
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Chronic Lymphocytic Leukemia (CLL)

Medicosis Perfectionalis - YouTube

👍 1 👎 0



Chronic leukaemia

Khan Academy - YouTube

👍 0 👎 0

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- 47 ✖
- 48 ✖
- 49 ✔
- 50 ✖



A 44-year-old male presents with a 2-month history of increasing lethargy. His wife reports him to be not quite himself for the past 2 months now, with poor oral intake and poor appetite. He is a self-employed software engineer but currently is unable to work due to his lethargy. He was previously treated for Hodgkin's lymphoma 5 years ago and has since been in remission.

On examination, he has no conjunctival pallor, is dry on his mucous membranes and extremely lethargic. Firm, rubbery lymph nodes are noted in the right axilla. Cardiovascular examination reveals a soft systolic murmur, respiratory and abdominal examinations are unremarkable. He is a non-smoker and drinks alcohol only occasionally. His blood tests are as follows:

Hb	88 g/l
MCV	104 fl
Platelets	$94 \times 10^9/l$
WBC	$12.8 \times 10^9/l$
Red cell distribution	9% (normal 11.5-14.5%)
Blood film	leucoerythroblastic with myeloblasts

What is the most likely cause of this patient's anaemia?

- ☐ B12 and folate deficiency ×
- ☐ Iron deficiency ×
- ☐ Anaemia of chronic disease ×
- ☐ Myelodysplasia post-chemotherapy ×
- ☐ Marrow infiltration ×

Submit answer

Reference ranges 

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MCV	104 fl
Platelets	94 * 10 ⁹ /l
WBC	12.8 * 10 ⁹ /l
Red cell distribution	9% (normal 11.5-14.5%)
Blood film	leucoerythroblastic with myeloblasts

What is the most likely cause of this patient's anaemia?

B12 and folate deficiency	10%
Iron deficiency	0%
Anaemia of chronic disease	2%
Myelodysplasia post-chemotherapy	53%
Marrow infiltration	35%

This patient has a symptomatic macrocytic anaemia, of which B12 and folate deficiency, myelodysplasia post-chemotherapy and marrow infiltration could all be causes. Iron deficiency results in a microcytic anaemia while anaemia of chronic disease typically causes a microcytic or normocytic anaemia. Blood cells in B12 and folate deficiency are typically megaloblastic, large immature red cells caused by impaired DNA synthesis. Myelodysplasia typically results in red cells of abnormal shapes (poikilocytosis) and sizes (anisocytosis) with Pappenheimer bodies (abnormal granules of iron). Chemotherapy is a possible cause of myelodysplasia but typically after recent treatment only. Sadly, in this case, the blood film of myeloblasts and erythroblasts suggests the transformation of Hodgkin's lymphoma into acute myeloid leukaemia, a well-recognised

complication of Hodgkin's lymphoma chemotherapy with older alkylating agents, typically 5 to 10 years after treatment. Blast cells have now subsequently infiltrated the bone marrow, resulting in macrocytic anaemia.

   Discuss (9)  Improve

[Next question >](#)

Macrocytic anaemia ★

Macrocytic anaemia can be divided into causes associated with a megaloblastic bone marrow and those with a normoblastic bone marrow








Megaloblastic causes of macrocytic anaemia

- vitamin B12 deficiency
- folate deficiency
- e.g. secondary to methotrexate

Normoblastic causes of macrocytic anaemia

- alcohol
- liver disease
- hypothyroidism
- pregnancy
- reticulocytosis
- myelodysplasia
- drugs: cytotoxics

[Next question >](#)

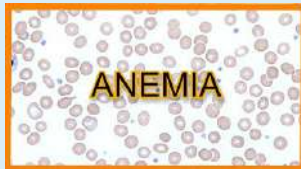
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Textbooks

High-yield textbook

Extended textbook

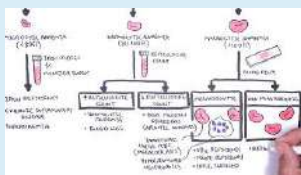
Media



Anemia (Types, Lab Findings, High Yield Images)

DirtyUSMLE - YouTube

👍 9 🗨️ 2



Anaemia (anemia) - classification (microcytic, normocytic and macrocytic) and pathophysiology

Armando Hasudungan - YouTube

👍 1 🗨️ 3

[Report broken media](#)

Score: **18%**

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Question 38 of 89



A 78-year-old gentleman with chronic lymphocytic leukaemia (CLL) presents with spontaneous bruising. He recalls no trauma and is otherwise well although he takes aspirin, simvastatin and ramipril for a previous myocardial infarction.

On examination, he looks well. His conjunctiva are pale but his chest is clear and he is warm and well perfused. A number of purpura are noted across the arms, back and chest. Palpable lymph nodes are felt in the left inguinal region. There is no hepatosplenomegaly.

Hb	104 g/l	Na ⁺	135 mmol/l
Platelets	54 * 10 ⁹ /l	K ⁺	4.0 mmol/l
WBC	10.3 * 10 ⁹ /l	Urea	3.4 mmol/l
Neuts	6.7 * 10 ⁹ /l	Creatinine	87 µmol/l
Lymphs	3.4 * 10 ⁹ /l	CRP	14 mg/l
Eosin	0.1 * 10 ⁹ /l		

What is the most appropriate management option?

- ☐ Suspend aspirin ×
- ☐ Start chlorambucil ×
- ☐ Start dexamethasone ×
- ☐ Platelet transfusion ×
- ☐ Splenectomy ×

Submit answer

Reference ranges 

Score: **16.1%**

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Question 38 of 89



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Neuts	6.7 * 10 ⁹ /l	Creatinine	87 µmol/l
Lymphs	3.4 * 10 ⁹ /l	CRP	14 mg/l
Eosin	0.1 * 10 ⁹ /l		

What is the most appropriate management option?

Suspend aspirin	26%
Start chlorambucil	41%
Start dexamethasone	24%
Platelet transfusion	4%
Splenectomy	4%

Thrombocytopenia -> indication to start treatment in CLL

Important for me Less important

This gentleman has developed thrombocytopenia on a background of CLL. This is an indication to start chemotherapy. In some cases, these may also respond to steroids but typically chemotherapy would be started and chlorambucil is a commonly used agent. Suspending aspirin will not fix thrombocytopenia but may be advised. There are no signs of hypersplenism as the cause of the thrombocytopenia. Platelet transfusion will not fix the underlying problem and is not urgent given there is no acute bleeding.

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (> 10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP


Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy


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
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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

 3  4

[2012 CLL guidelines](#)

[Suggest link](#)



[Report broken link](#)

Media



[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)



Medicosis Perfectionalis - YouTube

 3  2














[Chronic leukemia](#)

Osmosis - YouTube

 2  2

[Report broken media](#)

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49	✓



Question 39 of 89



A 30-year-old previously fit and well gentleman is injured following a road traffic accident after being thrown off his motorcycle. He was blue-lighted to the emergency department, where he was found to have multiple, profusely bleeding, lacerations of his extremities.

He was transfused 2 units of cross-matched blood, with no reactions detected in blood bank. Ten minutes after the transfusion, the patient developed severe urticaria.

Which of the following syndromes would contribute to the patient's picture?

- | | | |
|-----------------------|--------------------------------|---|
| <input type="radio"/> | Adenosine deaminase deficiency | × |
| <input type="radio"/> | Ataxia telangiectasia | × |
| <input type="radio"/> | DiGeorge syndrome | × |
| <input type="radio"/> | Selective IgA deficiency | × |
| <input type="radio"/> | Wiskott-Aldrich syndrome | × |

Submit answer

Reference ranges 

Score: **16.1%**

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Question 39 of 89



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He was transfused 2 units of cross-matched blood, with no reactions detected in blood bank. Ten minutes after the transfusion, the patient developed severe urticaria.

Which of the following syndromes would contribute to the patient's picture?

Adenosine deaminase deficiency	13%
Ataxia telangiectasia	2%
DiGeorge syndrome	3%
Selective IgA deficiency	73%
Wiskott-Aldrich syndrome	10%

IgA deficiency is associated with anaphylactic reaction to blood products

Important for me Less important

The majority of selective IgA deficiency patients are asymptomatic; with about 5% suffering from recurrent respiratory tract infections. The condition becomes clinically significant when blood transfusion is required, as there is the potential for anaphylaxis to occur on exposure to IgA containing blood products.

Although rare, anaphylaxis can happen from the first transfusion if the patient has been previously exposed to IgA i.e. in consumed animal meat products. If ever the patient needs a future blood transfusion, the transfused blood must be IgA free.



Discuss (1)

Improve

Next question >

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
Chronic granulomatous disease	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. <i>Staphylococcus aureus</i> and fungi (e.g. <i>Aspergillus</i>) Negative nitroblue-tetrazolium test Abnormal dihydrorhodamine flow cytometry test
Chediak-Higashi syndrome	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen Giant granules in neutrophils and platelets
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen Absence of neutrophils/pus at sites of infection

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Low antibody levels, specifically in immunoglobulin (Ig) types IgG, IgM and IgA. Recurrent chest infections. May also predispose to autoimmune disorders and lymphoma
Bruton's (x-linked) congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen Absence of B-cells with reduced immunoglobulins of all classes
Selective immunoglobulin A deficiency	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and

Disorder	Underlying defect	Notes
		<p>respiratory infections</p> <p>Associated with coeliac disease and may cause false negative coeliac antibody screen</p> <p>Severe reactions to blood transfusions may occur (anti-IgA antibodies → anaphylaxis)</p>

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4th pharyngeal pouches	Common features include congenital heart disease (e.g. tetralogy of Fallot), learning difficulties, hypocalcaemia, recurrent viral/fungal diseases, cleft palate

Combined B- and T-cell disorders


Disorder	Underlying defect	Notes
Severe combined immunodeficiency	Many varying causes. Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. Other causes include adenosine deaminase deficiency	<p>Recurrent infections due to viruses, bacteria and fungi.</p> <p>Reduced T-cell receptor excision circles</p> <p>Stem cell transplantation may be successful</p>
Ataxic telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia (spider angiomas), recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	<p>X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopenia.</p> <p>Low IgM levels</p>

Disorder	Underlying defect	Notes
		Increased risk of autoimmune disorders and malignancy
Hyper IgM Syndromes	Mutations in the CD40 gene	Infection/ <i>Pneumocystis</i> pneumonia, hepatitis, diarrhoea


Next question >

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Textbooks

High-yield textbook



Extended textbook

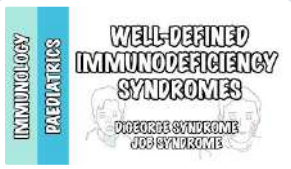
Media



[X linked agammaglobulinemia \(Bruton agammaglobulinemia\)](#)



Osmosis - YouTube

 1  0



[Well defined genetic immunodeficiency - DiGeorge Syndrome and Job Syndrome](#)

Armando Hasudungan - YouTube

 4  1



Leukocyte adhesion deficiency

Osmosis - YouTube

👍 4 👎 1



Selective immunoglobulin A deficiency

Osmosis - YouTube

👍 2 👎 1



Primary antibody deficiency - Common Variable Immunodeficiency (CVID) , X-linked agammaglobulinemia

Armando Hasudungan - YouTube

👍 2 👎 2



Digeorge syndrome (22q11.2 deletion syndrome)

Osmosis - YouTube

👍 0 👎 1

[Report broken media](#)

Score: **18%**

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Question 40 of 89



A 16-year-old female was admitted with new onset facial swelling. The facial swelling started 45 minutes ago and initially involved her lips. She complained of a sensation of choking and a feeling of being unable to speak with hoarseness of her voice. She had been investigated on multiple occasions for abdominal pain and was diagnosed with non-specific abdominal pain. She was not taking any medication and was otherwise healthy prior to the admission.

She was given prednisolone 40mg PO and chlorpheniramine 10mg PO and admitted for observation. Whilst in the department she developed profound shortness of breath with associated stridor. Her swelling around her lips worsened and involved the whole of her face. On examination, she was in respiratory distress with severe biphasic stridor. Her respiratory rate was 32/min with an oxygen saturation of 88% on air. Auscultation of her chest also revealed the presence of a widespread polyphonic wheeze. Examination of her cardiovascular system revealed the presence of flushed peripheries with a bounding peripheral pulse. Her pulse was 102bpm and her blood pressure was 92/68 mmHg. Her GCS was 15 and neurological and abdominal examinations were unremarkable. She was cannulated and commenced on stat intravenous colloid solution. She was given adrenaline 0.5mg IM on three separate occasions within 10 minutes with no improvement. She was transferred immediately to the Intensive Care Unit and an anaesthetist fast bleeped to secure her airway.

What is the best immediate management step pending definitive airway management?

- | | |
|---|---|
| <input type="radio"/> Commence IV adrenaline infusion | × |
| <input type="radio"/> Commence danazol | × |
| <input type="radio"/> Commence IV dopamine | × |
| <input type="radio"/> Commence fresh frozen plasma infusion | × |
| <input type="radio"/> Commence C1 esterase inhibitor concentrate infusion | × |

Submit answer

Reference ranges 

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7	✗
8	✗
9	✓
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What is the best immediate management step pending definitive airway management?

Commence IV adrenaline infusion	12%
Commence danazol	2%
Commence IV dopamine	1%
Commence fresh frozen plasma infusion	6%
Commence C1 esterase inhibitor concentrate infusion	79%

Hereditary angioedema: the acute management is IV C1-inhibitor concentrate or fresh frozen plasma if this is not available

Important for me Less important

This patient has hereditary angioedema. This condition is characterised by a lack of C1 esterase inhibitor and may present with laryngeal oedema, recurrent abdominal pain and localised subcutaneous swelling. Laryngeal oedema may be fatal, does not respond to glucocorticoids or antihistamines, and has an only modest response to adrenaline. The immediate management is to

commence C1 esterase inhibitor concentrate infusion. Fresh frozen plasma infusion may be administered if the concentrate is not available. Danazol is more suitable for subcutaneous oedema or as prophylaxis in certain situations eg prior to surgery.



Discuss (9)

Improve

Next question >

Hereditary angioedema ★

Hereditary angioedema (HAE) is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH, C1 esterase inhibitor) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

Symptoms

- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

Management

- acute
 - HAE does not respond to adrenaline, antihistamines, or glucocorticoids
 - IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links


Patient.info

Hereditary angioedema review

Suggest link

Report broken link

Media



The Role of the C1-Esterase Inhibitor in HAE

Individual - YouTube

3

0

Report broken media

Score: 18%

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An 18-year-old woman presents to the emergency department with two weeks of right upper quadrant pain. She also reported longstanding pain in her right femur. She has recently returned from a holiday in Tanzania.

On examination, there was mild tenderness in the right upper quadrant of the abdomen. There was hepatomegaly and splenomegaly detectable along with conjunctival pallor. She is afebrile. There is tenderness over the right femur.

Hb	91 g/L	Male: (135-180) Female: (115 - 160)
Platelets	112 * 10 ⁹ /L	(150 - 400)
WBC	4.2 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	5.3 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	12 µmol/L	(3 - 17)
ALP	88 u/L	(30 - 100)
ALT	32 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	36 g/L	(35 - 50)
LDH	512 U/L	(200-400)
Reticulocytes	43 * 10 ³ /L	(5-15)
Direct antiglobulin test	negative	(negative)
Haptoglobin	101 mg/dl	(50-220)

An ultrasound abdomen demonstrates massive splenomegaly (24 x 8 cm) and hepatomegaly.

An x-ray of the right femur demonstrates an Erlenmeyer flask deformity.

What is the likely diagnosis?

☐ Autoimmune haemolytic anaemia



<input type="radio"/>	Chronic myeloid leukaemia	×
<input type="radio"/>	Gaucher's disease	×
<input type="radio"/>	Malaria	×
<input type="radio"/>	Myelofibrosis	×

Submit answer

Reference ranges ▾

Score: **16.1%**

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An 18-year-old woman presents to the emergency department with two weeks of right upper quadrant pain. She also reported longstanding pain in her right femur. She has recently returned from a holiday in Tanzania.

On examination, there was mild tenderness in the right upper quadrant of the abdomen. There was hepatomegaly and splenomegaly detectable along with conjunctival pallor. She is afebrile. There is tenderness over the right femur.

Hb	91 g/L	Male: (135-180) Female: (115 - 160)
Platelets	112 * 10 ⁹ /L	(150 - 400)
WBC	4.2 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	5.3 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	12 µmol/L	(3 - 17)
ALP	88 u/L	(30 - 100)
ALT	32 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	36 g/L	(35 - 50)
LDH	512 U/L	(200-400)
Reticulocytes	43 * 10 ³ /L	(5-15)
Direct antiglobulin test	negative	(negative)
Haptoglobin	101 mg/dl	(50-220)

An ultrasound abdomen demonstrates massive splenomegaly (24 x 8 cm) and hepatomegaly.

An x-ray of the right femur demonstrates an Erlenmeyer flask deformity.

What is the likely diagnosis?

Autoimmune haemolytic anaemia

5%

Chronic myeloid leukaemia	6%
Gaucher's disease	64%
Malaria	13%
Myelofibrosis	13%

Gaucher disease causes splenomegaly

Important for me [Less important](#)

Gaucher's disease is the correct answer. The patient has hepatomegaly and massive splenomegaly along with anaemia and thrombocytopenia. While all of the options listed can cause splenomegaly, only Gaucher's disease is associated with constriction of the diaphysis and flaring of the metaphysis of the femur, resulting in a deformity known as the Erlenmeyer flask deformity (named because it resembles the conical flask used by chemists).

Autoimmune haemolytic anaemia is incorrect. This is a cause of mild rather than massive splenomegaly. Additionally, the negative direct antiglobulin test and haptoglobin make haemolysis unlikely.

Chronic myeloid leukaemia is incorrect. While this can cause hepatosplenomegaly and cytopenias, it is not associated with characteristic bone abnormalities like Gaucher disease. Additionally, it tends to present in older age rather than childhood/adolescence, like Gaucher's disease.

Malaria is incorrect. While she has travelled recently to Africa, she is afebrile and therefore this diagnosis is very unlikely.

Myelofibrosis is incorrect. This is another cause of massive splenomegaly. However, the characteristic bone abnormality in this condition is osteosclerosis. Additionally, it tends to present after the age of 60.




 Discuss (2)

 Improve

[Next question >](#)

Splenomegaly ★

Massive splenomegaly

- myelofibrosis
- chronic myeloid leukaemia

- visceral leishmaniasis (kala-azar)
- malaria
- Gaucher's syndrome

Other causes (as above plus)

- portal hypertension e.g. secondary to cirrhosis
- lymphoproliferative disease e.g. CLL, Hodgkin's
- haemolytic anaemia
- infection: hepatitis, glandular fever
- infective endocarditis
- sickle-cell*, thalassaemia
- rheumatoid arthritis (Felty's syndrome)

*the majority of adults patients with sickle-cell will have an atrophied spleen due to repeated infarction



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Score: **18%**

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- 49 ✔
- 50 ✖



A 72-year-old lady is on her third cycle of chemotherapy following mastectomy and axillary clearance of her left breast. She has a PICC line in situ through which she receives her chemotherapy. She developed chills and lethargy two days prior which led her to seek her GP who arranged admission to hospital. She has had one episode of diarrhoea and is currently being barrier nursed. Her swallowing is a problem due to odynophagia and she is only managing to take oral fluids.

She is currently taking G-CSF, omeprazole and dexamethasone. She has not travelled abroad and reports that she is excluding soft cheeses and pates from her diet.

On exam, she has a clear chest with no murmurs. There is *Candida* in the mouth and a temperature of 38.5°C recorded on admission. There are no wounds or rashes to be seen. She was started on broad-spectrum intravenous antibiotics and oral nystatin and admitted. You are asked to review her as she has spiked a fever of 39.8°C on her third day after admission and she is struggling to swallow fluids due to retrosternal pain.

Hb	96 g/l	Na ⁺	139 mmol/l
Platelets	123 * 10 ⁹ /l	K ⁺	5.1 mmol/l
WBC	1.6 * 10 ⁹ /l	Urea	4.5 mmol/l
Neuts	0.5 * 10 ⁹ /l	Creatinine	56 µmol/l
Lymphs	0.1 * 10 ⁹ /l	CRP	96 mg/l
Eosin	0.1 * 10 ⁹ /l		

Chest X-ray	clear lung fields, no effusion, no air under the diaphragm
Bloods cultures (1st peripheral)	no growth
Blood cultures (PICC line)	no growth
Blood cultures (2nd peripheral)	coagulase negative <i>staphylococcus</i>
Urine microscopy	no pyuria, no growth
Skin swab (PICC site)	awaited

What of the following is the most appropriate action?

Start metronidazole

5%

Start fluconazole

64%

Take a further set of blood cultures

17%

Increase dose of G-CSF

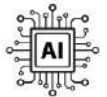
10%

Start paracetamol

3%

Neutropenic sepsis with no response to antibiotics at 48 hrs - > possible fungal infection

Important for me Less important



This lady has neutropenic sepsis of unknown source and has failed to improve despite broad-spectrum antibiotics. This prompts thoughts of what the cause could be. Increasing G-CSF may help her white cells increase but it does not treat the infection present. Paracetamol may reduce fevers but it does not treat the infection. Adding metronidazole is a reasonable thought since it covers anaerobic organisms and she has had a single episode of diarrhoea but the source of the sepsis is not clearly abdominal. Taking two sets of further blood cultures will be part of the workup needed but will not improve the patient's situation. Starting fluconazole is the answer. In any neutropenic sepsis, fungal causes should be considered especially if the patient does not improve on broad spectrum antibiotics. She has oral candida with odynophagia suggests possible oesophageal candidiasis. We should consider this especially given the *Candida* seen.



Discuss (9)

Improve

Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

NICE

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

[2012 Neutropenic sepsis guidelines](#)

Media



[Febrile Neutropenia](#)

Townsend Teaching - YouTube

 1  0

[What is febrile neutropaenia \(neutropenia\)? - neutrophil function, pathophysiology, treatment](#)








Armando Hasudungan - YouTube

 2  1

[Neutropenic sepsis](#)

Oncology for Medical Students - YouTube

 5  3[Report broken media](#)Score: **18%**

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| 50 | ✗ |



A 50-year-old woman presents to the emergency department with a 3-day history of headache and blurred vision. Despite taking co-codamol and ibuprofen, her headache has not been relieved and she has since started vomiting. She describes feeling generally unwell for the last 2-3 weeks with general malaise and body aches but denies fever and has no past medical history.

On examination, her visual acuity is reduced with noticeable nystagmus more pronounced on the left side. The remainder of her neurological examination is unremarkable.

Laboratory tests:

Hb	99 g/L	(115 - 160)
Platelets	150 * 10 ⁹ /L	(150 - 400)
WBC	38.3 * 10 ⁹ /L	(4.0 - 11.0)
Lymphs	3.2 * 10 ⁹ /L	(1.0 - 3.5)
Eosin	0.2 * 10 ⁹ /L	(0.0 - 0.4)
Na ⁺	136 mmol/L	(135 - 145)
K ⁺	3.8 mmol/L	(3.5 - 5.0)
Urea	6.2 mmol/L	(2.0 - 7.0)
Creatinine	90 µmol/L	(55 - 120)
Bilirubin	20 µmol/L	(3 - 17)
ALP	87 u/L	(30 - 100)
ALT	39 u/L	(3 - 40)
Albumin	38 g/L	(35 - 50)

What is the most likely diagnosis?

- ☐ Acute myeloid leukaemia ×
- ☐ Idiopathic intracranial hypertension ×
- ☐ Meningitis ×
- ☐ Multiple sclerosis ×
- ☐ Non-Hodgkin's lymphoma ×

Submit answer

Reference ranges 

Score: **16.1%**

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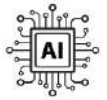
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Laboratory tests:

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Platelets	150 * 10 ⁹ /L	(150 - 400)
WBC	38.3 * 10 ⁹ /L	(4.0 - 11.0)
Lymphs	3.2 * 10 ⁹ /L	(1.0 - 3.5)
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Bilirubin	20 µmol/L	(3 - 17)
ALP	87 u/L	(30 - 100)
ALT	39 u/L	(3 - 40)
Albumin	38 g/L	(35 - 50)

What is the most likely diagnosis?

Acute myeloid leukaemia	74%
Idiopathic intracranial hypertension	5%
Meningitis	5%
Multiple sclerosis	3%
Non-Hodgkin's lymphoma	13%



This patient is presenting with hyperviscosity syndrome. Hyperviscosity syndrome is the increased viscosity of the blood caused by hyperproliferative states (e.g. leukaemia and polycythaemia), increased cell components (e.g. RBCs and WBCs) or increased immunoglobulins (e.g. multiple myeloma). Different bodily systems can be affected, but commonly the central nervous can be affected causing headaches, nystagmus and visual disturbance. This patient's blood results demonstrate a raised WBC count and a normal lymphocyte count, indicating that a large portion of the WBC is made of neutrophils, in keeping with a diagnosis of **acute myeloid leukaemia**. Additional symptoms of acute myeloid leukaemia include lethargy and malaise that are also described by this patient.

Idiopathic intracranial hypertension (IIH) is most common in women and is associated with obesity. It can present with a pressure-type headache with blurred vision. However, eye signs include 6th nerve palsy and papilloedema on fundoscopy. Furthermore, IIH does not explain this patient's raised WBC.

Meningitis can be secondary to a viral or bacterial infection. Presenting features typically include headache, fever and meningism. Vomiting and photophobia may also be seen. Although this patient has a raised WBC that could represent an underlying infection, meningitis does not typically cause nystagmus and the absence of fever and meningism also suggest an alternative diagnosis.

Multiple sclerosis is a demyelinating disease of the central nervous system. Common presenting symptoms include optic neuritis. Although a patient with multiple sclerosis could present with headache and nystagmus, it does not explain this patient's raised WBC.

Non-Hodgkin's lymphoma is a malignant proliferation of lymphocytes. It can present with malaise and hyperviscosity syndrome as described by this patient. However, additional symptoms include painless lymphadenopathy and constitutional symptoms such as night sweats and weight loss which are not described in this question. Furthermore, the presence of a normal lymphocyte count points towards an alternative diagnosis.

[Discuss \(6\)](#)[Improve](#)[Next question >](#)

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Features are largely related to bone marrow failure:

- anaemia: pallor, lethargy, weakness
- neutropenia: whilst white cell counts may be very high, functioning neutrophil levels may be low leading to frequent infections etc
- thrombocytopenia: bleeding
- splenomegaly
- bone pain

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- **Auer rods** (seen with myeloperoxidase stain)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)

- M0 - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic



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123



Next question >

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Textbooks

High-yield textbook

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Links

Clinical Knowledge Summaries

 7  11

[Haematological cancers - recognition and referral](#)

[Suggest link](#)

[Report broken link](#)

Media














[Acute myeloid & lymphoblastic leukemia](#)

Osmosis - YouTube

 9  1

[Report broken media](#)

Score: **18%**

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49	✓



A 44-year-old woman visits her general practitioner with a 10-day history of intermittent epistaxis. She has never had nosebleeds before but now says that even after blowing her nose, it will bleed for 2-3 minutes at a time. There is a past medical history of hypothyroidism for which she takes levothyroxine 75 micrograms daily. Other than recovering from influenza 3 weeks ago, she has had no recent illnesses.

On examination, she is afebrile. Her heart rate is 71bpm and regular with a blood pressure of 125/65mmHg. On auscultation, she has a clear chest with normal heart sounds. Her abdomen is soft and non-tender with no palpable organomegaly. There are multiple bruises and petechiae over her lower limbs and trunk.

Investigations:

Hb	116 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$16 \times 10^9/L$	(150 - 400)
WBC	$5.1 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	136 mmol/L	(135 - 145)
K ⁺	3.5 mmol/L	(3.5 - 5.0)
Urea	5.0 mmol/L	(2.0 - 7.0)
Creatinine	61 μ mol/L	(55 - 120)
Prothrombin time (PT)	12 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	28 secs	(25-35 secs)
Fibrinogen	2.6 g/L	(2 - 4)
D-Dimer	254 ng/mL	(< 400)

What is the most appropriate next step in this patient's management?

- ☐ Desmopressin ×
- ☐ Eltrombopag ×
- ☐ IV immunoglobulin ×
- ☐ Platelet transfusion ×
- ☐ Prednisolone ×

Submit answer

Reference ranges 

Score: **16.1%**

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Investigations:

Hb	116 g/L	Male: (135-180) Female: (115 - 160)
Platelets	16 * 10 ⁹ /L	(150 - 400)
WBC	5.1 * 10 ⁹ /L	(4.0 - 11.0)
Na ⁺	136 mmol/L	(135 - 145)
K ⁺	3.5 mmol/L	(3.5 - 5.0)
Urea	5.0 mmol/L	(2.0 - 7.0)
Creatinine	61 µmol/L	(55 - 120)
Prothrombin time (PT)	12 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	28 secs	(25-35 secs)
Fibrinogen	2.6 g/L	(2 - 4)
D-Dimer	254 ng/mL	(< 400)

What is the most appropriate next step in this patient's management?

Desmopressin	2%
Eltrombopag	1%
IV immunoglobulin	18%
Platelet transfusion	7%
Prednisolone	73%

This patient has immune thrombocytopenic purpura (ITP) the immune-mediated destruction of platelets. In ITP, autoantibodies are directed against glycoprotein IIb/IIIa or Ib-V-IX complexes and can be detected in up to 60-70%. The disease can develop acutely in children following a viral infection or vaccination and usually presents with mucocutaneous bleeding. There is also an association with autoimmune disease. ITP in children is often self-limiting compared to adults which tends to be more of a chronic condition with a relapsing-remitting course. This patient has a history of hypothyroidism and is recovering from a recent viral infection making ITP more likely. Features include easy bruising, epistaxis, purpura and menorrhagia. Massive haemorrhage is a rare complication. The treatment of choice is oral prednisolone at a dose of 1-2mg/kg. Approximately 80% respond to initial treatment.

Desmopressin is used in the treatment of Von-Willebrand's disease (VWD). VWD is a common inherited bleeding disorder that may first present as spontaneous mucocutaneous bleeding. It is caused by a deficiency in the von-Willebrand factor, a protein molecule that encourages platelet adhesion and binds to clotting factor VIII to prevent it from being broken down. A deficiency in this factor predisposes patients to increased bleeding. Blood tests in patients with VWD may demonstrate a microcytic anaemia, thrombocytopenia and a prolonged APTT (especially if factor VIII levels are reduced). However, this patient has never encountered issues with bleeding prior to a recent viral illness. This history combined with an isolated thrombocytopenia makes ITP the more likely diagnosis.

Eltrombopag is a thrombopoietin receptor agonist which acts to increase the platelet count. It is used as a 3rd-line treatment of ITP and is typically prescribed for chronic or refractory ITP.

IV immunoglobulin (IVIG) is another potential treatment option for ITP. It is commonly used in patients who fail to respond to corticosteroids or in patients for which corticosteroids are contraindicated. Another indication for IVIG is if a rapid rise in platelets is needed, for example prior to surgery.

Platelet transfusions are not the treatment of choice in ITP. They are reserved for extreme haemorrhage including intracranial haemorrhage.

[Discuss \(2\)](#)[Improve](#)[Next question >](#)

Immune thrombocytopenia (ITP) in adults ★

Immune (or idiopathic) thrombocytopenic purpura (ITP) is an immune-mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb/IIIa or Ib-V-IX complex.

Children with ITP usually have an acute thrombocytopenia that may follow infection or vaccination. In contrast, adults tend to have a more chronic condition.

ITP in adults

Epidemiology

- more common in older females

Presentation

- may be detected incidentally following routine bloods
- symptomatic patients may present with
 - petechiae, purpura
 - bleeding (e.g. epistaxis)
 - catastrophic bleeding (e.g. intracranial) is not a common presentation

Investigations

- full blood count: isolated thrombocytopenia
- blood film
- a bone marrow examination is no longer used routinely
- antiplatelet antibody testing has poor sensitivity and doesn't affect clinical management so is not commonly done

Management

- first-line treatment for ITP is oral prednisolone
- pooled normal human immunoglobulin (IVIG) may also be used
 - it raises the platelet count quicker than steroids, therefore may be used if active bleeding or an urgent invasive procedure is required
- splenectomy is now less commonly used

Evan's syndrome

- ITP in association with autoimmune haemolytic anaemia (AIHA)



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123



Next question >

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T



Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

👍 0 👎 1

[2003 ITP guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Bleeding Disorders \(ITP vs TTP vs HUS vs DIC\)](#)

Dirty USMLE - YouTube

👍 5 👎 0



[Immune thrombocytopenia \(ITP\)](#)

Osmosis - YouTube

👍 4 👎 0



[Thrombocytopaenia \(low platelets\) Overview - platelet physiology, classification, pathophysiology](#)

Armando Hasudungan - YouTube

👍 2 👎 1

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A 39-year-old man is referred to the haematology clinic by his GP due to abnormal blood results.

In the clinic, he reports a 2-week history of fatigue, malaise and intermittent abdominal pain. His past medical history includes anxiety and depression for which he takes citalopram. There is no history of smoking or recreational drug use although he drinks 6 cans of cider most evenings. He returned from a trip to India last month.

On examination, he appears lethargic. Chest auscultation is clear and his abdomen is soft with generalised tenderness.

Repeat blood tests are requested:

Hb	100 g/L	(135-180)
Mean Cell Volume	105 fL	(80 - 100)
Platelets	$100 \times 10^9/L$	(150 - 400)
WBC	$7.1 \times 10^9/L$	(4.0 - 11.0)
Bilirubin	80 $\mu\text{mol/L}$	(3 - 17)
ALP	118 u/L	(30 - 100)
ALT	40 u/L	(0 - 40)
AST	65 u/L	(< 35)
Blood glucose	6.1 mmol/L	(4 - 7)
Total cholesterol	7.3 mmol/L	(< 5)

Further investigations are sent:

Blood film	Schistocytes
Coombs test	Negative

What is the most appropriate management for this patient?

- ☐ Alcohol cessation ×
- ☐ Artesunate ×
- ☐ Blood transfusion ×

☐ Intravenous immunoglobulin (IVIg)



☐ Prednisolone



Submit answer

Reference ranges

Score: **16.1%**

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Blood glucose	6.1 mmol/L	(4 - 7)
Total cholesterol	7.3 mmol/L	(< 5)

Further investigations are sent:

Blood film	Schistocytes
Coombs test	Negative

What is the most appropriate management for this patient?

Alcohol cessation	56%
Artesunate	18%
Blood transfusion	2%

Intravenous immunoglobulin (IVIg)

12%

Prednisolone

13%

Zieve syndrome usually resolves with abstinence from alcohol

Important for me **Less important**

Alcohol cessation is correct. This patient has a likely diagnosis of Zieve syndrome given the triad of non-autoimmune haemolysis, jaundice and hyperlipidaemia on a background of alcohol excess. The negative Coombs test indicates non-autoimmune haemolytic anaemia. In Zieve syndrome, jaundice can be cholestatic in nature but also secondary to haemolysis. The raised ALP supports a cholestatic picture. Zieve syndrome is a rare syndrome and generally resolves following the cessation of alcohol use.

Artesunate is incorrect. Another differential diagnosis for haemolytic anaemia includes infective causes such as malaria. Although this patient has recently travelled to India, the majority of India is relatively malaria-free in comparison to other parts of the world. It also does not account for the raised triglyceride level and cholestatic jaundice.

Blood transfusion is incorrect. Generally, the threshold for blood transfusion is a Hb < 70g/dL or < 80g/dL if the patient has ischaemic heart disease. It would not treat this patient's underlying diagnosis.

Intravenous immunoglobulin (IVIg) is incorrect. This can be used to treat autoimmune haemolytic anaemia and other haematological conditions such as immune thrombocytopenic purpura. However, the negative Coombs test makes autoimmune haemolytic anaemia highly unlikely.

Prednisolone is incorrect. Like IVIg, prednisolone is used in the treatment of autoimmune haemolytic anaemia. This is unlikely to be the underlying diagnosis since the Coombs test is negative. Therefore, other causes of haemolytic anaemia should be considered and investigated.



Discuss (5)

Improve

Next question >

Haemolytic anaemias: by cause ★

Hereditary haemolytic anaemias can be subdivided into membrane, metabolism or haemoglobin defects

Hereditary causes

- membrane: hereditary spherocytosis/elliptocytosis
- metabolism: G6PD deficiency
- haemoglobinopathies: sickle cell, thalassaemia

Acquired haemolytic anaemias can be subdivided into immune and non-immune causes

Acquired: immune causes (Coombs-positive)

- autoimmune: warm/cold antibody type
- alloimmune: transfusion reaction, haemolytic disease newborn
- drug: methyldopa, penicillin

Acquired: non-immune causes (Coombs-negative)

- microangiopathic haemolytic anaemia (MAHA): TTP/HUS, DIC, malignancy, pre-eclampsia
- prosthetic heart valves
- paroxysmal nocturnal haemoglobinuria
- infections: malaria
- drug: dapsone
- Zieve syndrome
 - rare clinical syndrome of Coombs-negative haemolysis, cholestatic jaundice, and transient hyperlipidaemia associated with heavy alcohol use, typically following a binge
 - typically resolves with abstinence from alcohol



123



Next question >

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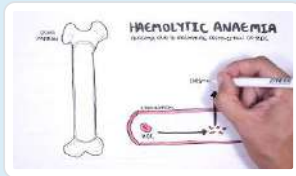


Textbooks

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Media



Haemolytic Anaemia - classification (intravascular, extravascular), pathophysiology, investigations

Armando Hasudungan - YouTube

👍 3 👎 2

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Question 46 of 89



A 59-year-old man suddenly becomes unwell on the oncology unit. He is receiving an intravenous infusion of a new chemotherapy agent as part of a clinic trial. He says he feels very lightheaded. On examination his blood pressure is 80/50 mmHg, heart rate is 120/min, oxygen saturations are 94% on air and bilateral wheeze is heard on auscultation of the chest. An ECG shows a sinus tachycardia of 120 beats per minute. The infusion is stopped, the patient is lay flat with their legs raised and an arrest call has been put out.

What should you administer immediately?

- ☐ 0.5mL of 1:1000 intramuscular adrenaline ×
- ☐ 0.5mL of 1:10000 intramuscular adrenaline ×
- ☐ 0.5mL of 1:1000 intravenous adrenaline ×
- ☐ 0.5mL of 1:10000 intravenous adrenaline ×
- ☐ 1mL of 1:10000 intravenous adrenaline ×

Submit answer

Reference ranges 

Score: **16.1%**

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What should you administer immediately?

0.5mL of 1:1000 intramuscular adrenaline	68%
0.5mL of 1:10000 intramuscular adrenaline	13%
0.5mL of 1:1000 intravenous adrenaline	9%
0.5mL of 1:10000 intravenous adrenaline	3%
1mL of 1:10000 intravenous adrenaline	7%

Anaphylaxis - adult adrenaline dose = 500 mcg (0.5 ml of 1 in 1,000)

Important for me Less important

This patient is having an anaphylactic reaction to the infusion. Essential immediate management of anaphylaxis comprises: recognition that the patient is seriously unwell, removal of the trigger (if possible), an early call for help, assessment via the ABCDE (airway, breathing, circulation, disability, exposure) approach and administration of adrenaline.

The correct dose of adrenaline in anaphylaxis via the intramuscular route is 0.5mL of 1:1000 (1mg in 1mL/ 0.5mg in 0.5mL). Adrenaline should usually be administered via the intramuscular route as there is a lower risk of inappropriate administration, the incidence of adverse effects is rare, it is an easy method to learn and IV access is not required. Inappropriate intravenous administration risks precipitating arrhythmias, which may result in cardiac arrest. Specialists such as anaesthetists may use the intravenous route, but for the majority of practitioners the intramuscular route is the best option.

As soon as possible after or concurrently with the administration of adrenaline; high-flow oxygen and a rapid intravenous fluid challenge should be delivered. Subsequent to this, an intravenous or intramuscular antihistamine (e.g. chlorphenamine) and steroid (e.g. hydrocortisone) may be given.

Source:

Emergency treatment of anaphylactic reactions (Resuscitation council UK guidelines)
<https://www.resus.org.uk/anaphylaxis/emergency-treatment-of-anaphylactic-reactions/>



Next question >

Anaphylaxis ★

Anaphylaxis may be defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction.

Common identified causes of anaphylaxis:

- food (e.g. nuts) - the most common cause in children
- drugs
- venom (e.g. wasp sting)

Features

The Resus Council UK define anaphylaxis as:

- the sudden onset and rapid progression of symptoms
- **A**irway and/or **B**reathing and/or **C**irculation problems
- **A**irway problems may include:
 - swelling of the throat and tongue → hoarse voice and stridor
- **B**reathing problems may include:
 - respiratory wheeze
 - dyspnoea
- **C**irculation problems may include:
 - hypotension
 - tachycardia

This means that if there are no ABC problems then the patient is technically not having anaphylaxis.

Around 80-90% of patients also have skin and mucosal changes:

- generalised pruritus
- widespread erythematous or urticarial rash

Anaphylaxis is one of the few times when you would not have time to look up the dose of a medication. The Resuscitation Council guidelines on anaphylaxis have recently been updated. **Intramuscular adrenaline** is by far the most important drug in anaphylaxis and should be given as soon as possible. Previously IV hydrocortisone was also recommended but the evidence base for this was poor and it was removed in the 2021 update.

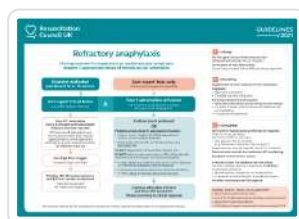
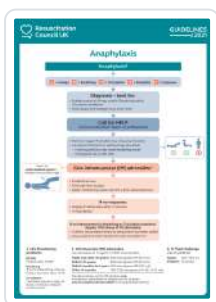
The recommended doses for adrenaline are as follows: **BNF**

Age	Adrenaline dose
< 6 months	100 - 150 micrograms (0.1 - 0.15 ml 1 in 1,000)
6 months - 6 years	150 micrograms (0.15 ml 1 in 1,000)
6-12 years	300 micrograms (0.3ml 1 in 1,000)
Adult and child > 12 years	500 micrograms (0.5ml 1 in 1,000)

Adrenaline can be repeated every 5 minutes if necessary. The best site for IM injection is the anterolateral aspect of the middle third of the thigh.

Refractory anaphylaxis

- defined as respiratory and/or cardiovascular problems persist despite 2 doses of IM adrenaline
- IV fluids should be given for shock
- expert help should be sought for consideration of an IV adrenaline infusion



Management following stabilisation:

- non-sedating oral antihistamines, in preference to chlorphenamine, may be given following initial stabilisation especially in patients with persisting skin symptoms (urticaria and/or angioedema)
- sometimes it can be difficult to establish whether a patient had a true episode of anaphylaxis. Serum tryptase levels are sometimes taken in such patients as they remain elevated for up to 12 hours following an acute episode of anaphylaxis
- all patients with a new diagnosis of anaphylaxis should be referred to a specialist allergy clinic

- an adrenaline injector should be given as an interim measure before the specialist allergy assessment (unless the reaction was drug-induced)
 - patients should be prescribed 2 adrenaline auto-injectors
 - training should be provided on how to use it
- a risk-stratified approach to discharge should be taken as biphasic reactions can occur in up to 20% of patients

The Resus Council UK recommend the following risk-stratified approach to discharge:

- fast-track discharge (after 2 hours of symptom resolution):
 - good response to a single dose of adrenaline
 - complete resolution of symptoms
 - has been given an adrenaline auto-injector and trained how to use it
 - adequate supervision following discharge
- minimum 6 hours after symptom resolution
 - 2 doses of IM adrenaline needed, or
 - previous biphasic reaction
- minimum 12 hours after symptom resolution
 - severe reaction requiring > 2 doses of IM adrenaline
 - patient has severe asthma
 - possibility of an ongoing reaction (e.g. slow-release medication)
 - patient presents late at night
 - patient in areas where access to emergency care may be difficult
 - observation for at 12 hours following symptom resolution



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

Clinical Knowledge Summaries

👍 1 🗑️ 0

[Angio-oedema and anaphylaxis](#)

Resus Council

👍 3 🗑️ 1

[Anaphylaxis guidelines](#)

BNF

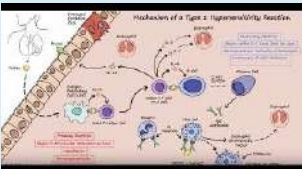
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[Medical emergencies in the community](#)

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Media



[Type I Hypersensitivity](#)

PhysioPathoPharmaco - YouTube 👍 3 🗑️ 2



[Type I hypersensitivity](#)

Osmosis - YouTube 👍 1 🗑️ 1

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Question 47 of 89



A 24-year-old male is admitted with shortness of breath. On examination his respiratory rate is 34 breaths per minute and heart rate is 125 beats per minute. His blood pressure is 120/85 mmHg. An SpO₂ reading is 84%. He looks cyanotic. He has a past medical history of coeliac disease, dermatitis herpetiformis, rheumatoid arthritis and asthma. His regular medicines include dapsone, prednisolone, paracetamol and ibuprofen. He just recently completed a course of amoxicillin for a chest infection.

An arterial blood gas is performed (on 15 litres of O₂):

Hb	125 g/l
pH	7.33
PaO ₂	58.11 kPa
PaCO ₂	2.48 kPa
SO ₂	99.7%
HCO ₃	12 mmol/l

What drugs is most likely implicated?

☐ Dapsone
 ×

☐ Amoxicillin
 ×

☐ Prednisolone
 ×

☐ Ibuprofen
 ×

☐ Paracetamol
 ×

Submit answer

Reference ranges 

Score: **16.1%**

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An arterial blood gas is performed (on 15 litres of O₂):

Hb	125 g/l
pH	7.33
PaO ₂	58.11 kPa
PaCO ₂	2.48 kPa
SO ₂	99.7%
HCO ₃	12 mmol/l

What drugs is most likely implicated?

Dapsone	88%
Amoxicillin	4%
Prednisolone	2%
Ibuprofen	6%
Paracetamol	1%

Dapsone + dyspnoea → methaemoglobinaemia

Important for me Less important

Several inferences should be made with regards to the blood gas. The PaO₂ is appropriately high given the patient is on 15L of O₂. A simple way of estimating an appropriate PaO₂ is to multiple the % of inspired O₂ (FiO₂) by 2/3. For example, 15L of O₂ driven by a non-rebreather mask delivers approximately 90% of O₂. Therefore we would expect the PaO₂ to be is approximately $\frac{2}{3} * 90 = 60$ kPa. The patient in this example has a PaO₂ of 62.22 kPa. Therefore we can confidently state that gas exchange at the level of the alveoli is not the cause of the cyanosis. It is important to

remember that the PaO₂ is a measure of dissolved O₂ in blood. Oxygen is carried in the blood in two forms: dissolved in plasma (about 2% of the total) and reversibly bound to haemoglobin (about 98% of the total). Therefore alternative causes for the cyanosis should be sought e.g. anaemia, shock, and toxic causes (e.g. methemoglobinemia).

The saturation of Hb on the ABG (SaO₂) is 99.7%. This is strange as there is a large discrepancy between this and the peripheral pulse oximeter result (86%). This should alert you to consider two differentials - carbon monoxide poisoning and methemoglobinemia. The SaO₂ on the blood gas machine is broken down to several components - O₂Hb (the 'true' saturation of Hb with O₂), COHb (carboxyhemoglobin), HHb, and MetHb. The sum of all these components produces the total saturation SaO₂. In this case, the patient has a significantly high MetHb confirming the diagnosis of methemoglobinemia. The true oxygen saturation is 55.3%. This is the cause of the hypoxia and the resultant lactic acidosis.

Methemoglobinemia describes haemoglobin which has been oxidised from Fe²⁺ to Fe³⁺. Fe³⁺ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left. This results in tissue hypoxia. Drugs (e.g. sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine) are common causes. Dapsone is a common cause of methemoglobinemia.

None of the other agents are known to cause methemoglobinemia.

		 Discuss (7)	Improve
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Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe²⁺ to Fe³⁺. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe³⁺ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO₂ but decreased oxygen saturation

Management

- NADH methaemoglobinemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



123



Next question >

B

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Textbooks

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Links

Life in the Fast Lane

6 3

[Methaemoglobinemia](#)

The Internet Book of Critical Care

10 4

[Methemoglobinemia](#)

[Suggest link](#)

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Media



Methaemoglobinaemia

Osmosis - YouTube 7 2

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A 64-year-old man presents to the haematology clinic with a history of back pain over the past 6 months. On systematic enquiry and examination, there are no features of spinal cord compression or cauda equina syndrome.

Blood results are as follows:

Hb	110 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$165 \times 10^9/L$	(150 - 400)
WBC	$6.2 \times 10^9/L$	(4.0 - 11.0)
Na ⁺	135 mmol/L	(135 - 145)
K ⁺	4.8 mmol/L	(3.5 - 5.0)
Urea	10.8 mmol/L	(2.0 - 7.0)
Creatinine	190 $\mu\text{mol/L}$	(55 - 120)

Protein electrophoresis	Monoclonal IgG 38g/l
-------------------------	----------------------

Given the likely diagnosis, what is the imaging modality of choice?

- ☐ CT PET ×
- ☐ No imaging required ×
- ☐ Plain film skeletal survey ×
- ☐ Whole body MRI ×
- ☐ Whole body low-dose CT ×

Submit answer

Reference ranges 

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Creatinine	190 µmol/L	(55 - 120)

Protein electrophoresis	Monoclonal IgG 38g/l
-------------------------	----------------------

Given the likely diagnosis, what is the imaging modality of choice?

CT PET

3%

No imaging required

2%

Plain film skeletal survey

9%

Whole body MRI

83%

Whole body low-dose CT

3%

Whole body MRI 1st line imaging in suspected multiple myeloma

Important for me

Less important

The clinical features (e.g. back pain, anaemia, renal dysfunction), and the presence of a paraprotein make multiple myeloma the most likely diagnosis.

Whole body MRI is recommended as the first-line imaging modality in multiple myeloma. MRI is the most sensitive tool available for detecting marrow infiltration at an early stage, before bone

destruction occurs, as well as offering improved detection of lesions, particularly in the axial skeleton.

Skeletal survey is incorrect. The major disadvantage of plain X-rays is the significantly lower sensitivity compared to advanced imaging. Lytic lesions are only demonstrated when at least 30-50% of the trabecular bone has been lost and around 20% of myeloma patients have no abnormal findings by plain X-ray. Plain X-rays cannot distinguish osteopenia or vertebral collapse caused by myeloma from more common causes such as early osteoporosis or corticosteroid use. For these reasons - skeletal surveys with plain X-rays are no longer recommended.

CT skeletal survey is incorrect. From a practical point of view, CT has the advantage of being quick to perform and allows patients to lie on their back, without the need to change position. CT is also helpful for visualising soft tissue involvement, assessing spinal fracture stability, depicting spinal cord and cauda equina compression (although MRI is superior for this), guiding needle biopsies and surgical interventions, and planning radiotherapy. However, MRI remains the gold standard.

FDG PET/CT is incorrect. PET may be considered for patients with newly diagnosed nonsecretory or oligosecretory myeloma and for evaluation of extramedullary disease. Although FDG PET/CT has some prognostic value when used in the initial diagnosis of myeloma, there is currently insufficient evidence to justify the routine use of FDG PET/CT in all cases of newly diagnosed myeloma.

No imaging required is incorrect. The patient most certainly has a new diagnosis of multiple myeloma and thus cross-sectional imaging is required.

   Discuss (1) [Improve](#)

[Next question >](#)

Myeloma: features and investigation ★

Multiple myeloma (MM) is a haematological malignancy characterised by plasma cell proliferation. It arises due to genetic mutations which occur as B-lymphocytes differentiate into mature plasma cells.

Features

The median age at presentation is 70 years old.

Use the mnemonic **CRABBI**:

- Calcium
 - hypercalcaemia

- primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
- much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
- this leads to constipation, nausea, anorexia and confusion
- Renal
 - monoclonal production of immunoglobulins results in light chain deposition within the renal tubules
 - this causes renal damage which presents as dehydration and increasing thirst
 - other causes of renal impairment in myeloma include amyloidosis, nephrocalcinosis, nephrolithiasis
- Anaemia
 - bone marrow crowding suppresses erythropoiesis leading to anaemia
 - this causes fatigue and pallor
- Bleeding
 - bone marrow crowding also results in thrombocytopenia which puts patients at increased risk of bleeding and bruising
- Bones
 - bone marrow infiltration by plasma cells and cytokine-mediated osteoclast overactivity creates lytic bone lesions
 - this may present as pain (especially in the back) and increases the risk of pathological fractures
- Infection
 - a reduction in the production of normal immunoglobulins results in increased susceptibility to infection

Other features include

- amyloidosis e.g. macroglossia
- carpal tunnel syndrome
- neuropathy
- hyperviscosity

Investigations

Bloods

- full blood count: anaemia
- peripheral blood film: rouleaux formation
- urea and electrolytes: renal failure
- bone profile: hypercalcaemia

Protein electrophoresis

- raised concentrations of monoclonal IgA/IgG proteins will be present in the serum
- in the urine, they are known as Bence Jones proteins

Bone marrow aspiration

- confirms the diagnosis if the number of plasma cells is significantly raised

Imaging

- historically a skeletal survey has been done to look for bone lesions
- however, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

Diagnostic criteria

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria

- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria

- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).
- Low levels of antibodies (not produced by the cancer cells) in the blood.



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123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

Clinical Knowledge Summaries

 10  10

[Haematological cancers - recognition and referral](#)

NICE

 12  6

[2016 myeloma guidelines](#)

[Suggest link](#)



[Report broken link](#)

Media



[Multiple Myeloma - Diagnosis and Treatment](#)


Medicosis Perfectionalis - YouTube

 6  0



[Multiple Myeloma](#)

Medicosis Perfectionalis - YouTube

 4  0



[Multiple Myeloma Mnemonic...the story of the plasma cell](#)

Medicosis Perfectionalis - YouTube

 5  1



What is multiple myeloma?

Khan Academy - YouTube

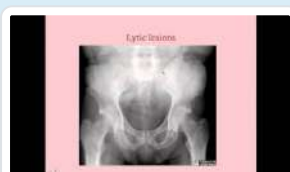
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Multiple Myeloma

Townsend Teaching - YouTube

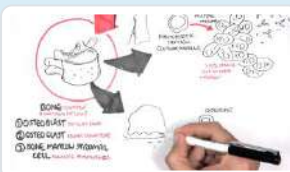
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Multiple Myeloma

CRASH! Medical Review - YouTube

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Multiple Myeloma

Armando Hasudungan - YouTube

👍 1 🗨️ 3

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A 22-year-old man is seen in the general medical clinic. He has had several episodes of gallstones over the last three months. He is due to see the surgical team for consideration of laparoscopic cholecystectomy but he was also referred to the medical team due to anaemia. He has needed blood transfusions in the past when he has become tired and found to be anaemic. He was referred for an appointment with a haematologist but was unable to attend and therefore discharged from the clinic without seeing the consultant. He takes no regular tablets. He is unaware of any family history of significant medical problems, but does think that his mother used to turn yellow when slightly unwell, but thinks that this has never been a serious medical problem. He also knows that his father, to whom he is estranged, had some medical problem with his blood. His observations are normal as is his examination apart from conjunctival pallor and 2cm of a palpable spleen.

Blood tests:

Hb	110 g/l
MCV	84.1 fl
MCHC (mean corpuscular haemoglobin concentration)	391 g/l
Platelets	$389 \times 10^9/l$
WBC	$8.2 \times 10^9/l$
Na ⁺	138 mmol/l
K ⁺	4.8 mmol/l
Urea	5.2 mmol/l
Creatinine	85 μ mol/l
Bilirubin	22 μ mol/l
ALP	42 u/l
ALT	15 u/l

What is the most likely underlying diagnosis?

- ☐ Sickle cell disease ×
- ☐ Pernicious anaemia ×
- ☐ Glucose-6-phosphate dehydrogenase (G6PD) deficiency ×
- ☐ Thalassaemia ×

☐ Hereditary spherocytosis



Submit answer

Reference ranges

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Bilirubin	22 µmol/l
ALP	42 u/l
ALT	15 u/l

What is the most likely underlying diagnosis?

Sickle cell disease	5%
Pernicious anaemia	1%
Glucose-6-phosphate dehydrogenase (G6PD) deficiency	16%
Thalassaemia	6%

Hereditary spherocytosis is an explanation for anaemia in recurrent gallstones

Important for me **Less important**

This young man has a history of anaemia with recurrent gallstones. This implies that there has been destruction of red blood cells and the subsequent rise in bilirubin has provoked the formation of gallstones. The presence of normocytic anaemia with elevated MCHC further supports a diagnosis of spherocytosis. The family history of potentially Gilbert's syndrome would raise the possibility of the patient having this diagnosis as well, which would increase the possibility of gallstones in spherocytosis. The presence of splenomegaly supports this diagnosis. Diagnosis would be confirmed with microscopy and osmotic fragility testing. Pernicious anaemia would be macrocytic and would not be associated with haemolysis. Sickle cell disease would clinically have severe haemolytic normocytic anaemia, recurrent infections and vaso-occlusive phenomena. The absence of such episodes and age of presentation makes sickle cell disease unlikely. In addition, it is screened for in the UK and routinely diagnosed in the neonatal setting. G6PD is a X-linked cause of haemolytic anaemia triggered commonly by drugs causing acute episodes of haemolysis. The absence of a neonatal history of jaundice and demographic risk factors, as well as no trigger makes this less likely, as does the presence of splenomegaly. Thalassaemia would not cause splenomegaly or gallstones.



Discuss (12)

Improve

Next question >

Hereditary spherocytosis ★

Basics

- most common hereditary haemolytic anaemia in people of northern European descent
- autosomal dominant defect of red blood cell cytoskeleton
- the normal biconcave disc shape is replaced by a sphere-shaped red blood cell
- red blood cell survival reduced as destroyed by the spleen

Presentation

- failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable
- MCHC elevated

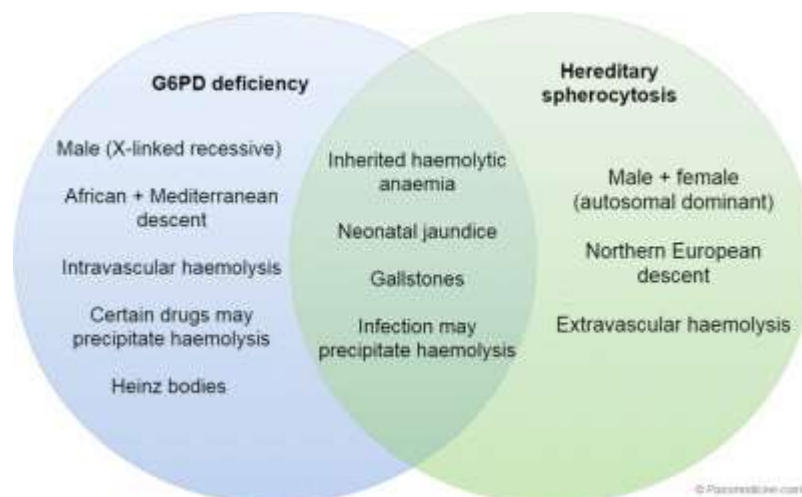
Diagnosis

- the osmotic fragility test was previously the recommended investigation of choice. However, it is now deemed unreliable and is no longer recommended
- the British Journal of Haematology (BJH) guidelines state that '*patients with a family history of HS, typical clinical features and laboratory investigations (spherocytes, raised mean corpuscular haemoglobin concentration [MCHC], increase in reticulocytes) do not require any additional tests*
- if the diagnosis is equivocal the BJH recommend the EMA binding test and the cryohaemolysis test
- for atypical presentations electrophoresis analysis of erythrocyte membranes is the method of choice

Management

- acute haemolytic crisis:
 - treatment is generally supportive
 - transfusion if necessary
- longer term treatment:
 - folate replacement
 - splenectomy

Comparing G6PD deficiency to hereditary spherocytosis:



Comparison of G6PD deficiency to hereditary spherocytosis

	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent

	G6PD deficiency	Hereditary spherocytosis
Typical history	<ul style="list-style-type: none"> • Neonatal jaundice • Infection/drugs precipitate haemolysis • Gallstones 	<ul style="list-style-type: none"> • Neonatal jaundice • Chronic symptoms although haemolytic crises may be precipitated by infection • Gallstones • Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	EMA binding test



123



Next question >

B

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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

2011 Hereditary spherocytosis guidelines

14

7

Suggest link

Report broken link

Media



3



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[Report broken media](#)

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A 32-year-old woman is on her second cycle of chemotherapy for breast cancer. She has developed two days of watery diarrhoea and vomiting. She has occasional chills and feels generally weak. She has not travelled abroad and there are no ill contacts. Her husband is a farmer and together they attended a farm foods show which hosted local cheese and meats in the local region.

On examination, she has a soft abdomen that is mildly tender in the right iliac fossa. Her mucosa is dry and she is achy in muscle groups throughout her body.

Hb	110 g/l	Na ⁺	138 mmol/l
Platelets	348 * 10 ⁹ /l	K ⁺	3.9 mmol/l
WBC	2.4 * 10 ⁹ /l	Urea	4.3 mmol/l
Neuts	0.7 * 10 ⁹ /l	Creatinine	76 µmol/l
Lymphs	1.4 * 10 ⁹ /l	CRP	96 mg/l

Stool specimen	gram-positive bacillus
----------------	------------------------

What is the causative organism in this case?

- ☐ Listeriosis ×
- ☐ Salmonellosis ×
- ☐ Shigellosis ×
- ☐ *Clostridium perfringens* poisoning ×
- ☐ *Staphylococcus aureus* poisoning ×

Submit answer

Reference ranges 

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Lymphs	1.4 * 10 ⁹ /l	CRP	96 mg/l

Stool specimen	gram-positive bacillus
----------------	------------------------

What is the causative organism in this case?

Listeriosis	63%
Salmonellosis	7%
Shigellosis	3%
<i>Clostridium perfringens</i> poisoning	20%
<i>Staphylococcus aureus</i> poisoning	6%

Neutropenic patients should avoid soft cheese due to risk of listeriosis

Important for me Less important

This is a case of neutropenic sepsis. Patients are at high risk to many organisms and it is suggested they avoid cold meats and dairy products. She had gastrointestinal symptoms and cultured a gram-positive bacillus. This immediately rules out salmonellosis and shigellosis. The gram-positive is a bacillus so cannot be *staphylococcus*. Of the two remaining, only *listeria* is found in dairy products and therefore is the likely cause of her illness



Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients





Textbooks

High-yield textbook

Extended textbook



Links

NICE

 3  1

[2012 Neutropenic sepsis guidelines](#)

Christies

 2  4

[2013 Neutropenic sepsis guidelines](#)

[Suggest link](#)



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Media



[Febrile Neutropenia](#)



Townsend Teaching - YouTube

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[What is febrile neutropaenia \(neutropenia\)? - neutrophil function, pathophysiology, treatment](#)

Armando Hasudungan - YouTube

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Neutropenic sepsis

Oncology for Medical Students - YouTube

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A 22-year-old woman awaiting stem cell transplant for acute myeloid leukaemia has become unwell over the past three days and arrives with a Glasgow Coma Scale of 3 in the emergency department. Her boyfriend who is present with her reports that she has had severe headaches and been sitting in bed but gradually became more confused. She was struggling to breathe and began to seize causing him to call the ambulance.

On examination, she is intubated and has bilateral coarse crepitations. Her pupils are reactive but she is sedated and does not respond to pain. There is papilloedema bilaterally and haemorrhages are seen in the left eye. She is warm and well perfused but her left arm is cold and pale. She is transferred to the intensive care unit.

Hb	120 g/l
Platelets	350 * 10 ⁹ /l
WBC	105 * 10 ⁹ /l
Troponin	10,876 (normal range <20)
CRP	56 mg/l
Chest x-ray	bilateral pulmonary infiltrates, small left sided effusion

What medical treatment will correct her underlying pathology should be initiated?

- ☐ Intravenous antibiotics ×
- ☐ High dose corticosteroids ×
- ☐ Leukapheresis ×
- ☐ High dose chemotherapy ×
- ☐ Venesection ×

Submit answer

Reference ranges 

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Question 51 of 89



A 22-year-old woman awaiting stem cell transplant for acute myeloid leukaemia has become unwell over the past three days and arrives with a Glasgow Coma Scale of 3 in the emergency department. Her boyfriend who is present with her reports that she has had severe headaches and been sitting in bed but gradually became more confused. She was struggling to breathe and began to seize causing him to call the ambulance.

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Hb	120 g/l
Platelets	350 * 10 ⁹ /l
WBC	105 * 10 ⁹ /l
Troponin	10,876 (normal range <20)
CRP	56 mg/l
Chest x-ray	bilateral pulmonary infiltrates, small left sided effusion

What medical treatment will correct her underlying pathology should be initiated?

Intravenous antibiotics	3%
High dose corticosteroids	16%
Leukapheresis	70%
High dose chemotherapy	6%
Venesection	6%

Leukapheresis can be used to acutely lower the white cell count in AML

Important for me Less important

This lady presents with pulmonary oedema and neurological dysfunction on a background of hyperleukocytosis. This is leukostasis where the blood is thick in white cells. The treatment is to rapidly remove white cells. This can be done by leukapheresis of the blood and removing the white cells which is called leukapheresis and this is the most appropriate answer. Venesection and

high dose chemotherapy are less effective ways of achieving a lower white cell count. Corticosteroids and antibiotics will not help.



Discuss (6)

Improve

Next question >

Acute myeloid leukaemia ★

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Features are largely related to bone marrow failure:

- anaemia: pallor, lethargy, weakness
- neutropenia: whilst white cell counts may be very high, functioning neutrophil levels may be low leading to frequent infections etc
- thrombocytopenia: bleeding
- splenomegaly
- bone pain

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- Auer rods (seen with myeloperoxidase stain)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)

- M0 - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic



123

[Next question >](#)**B***I***A****T**

Textbooks

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Links

[Clinical Knowledge Summaries](#)

7



11

[Haematological cancers - recognition and referral](#)[Suggest link](#)[Report broken link](#)

Media

[Acute myeloid & lymphoblastic leukemia](#)[Osmosis - YouTube](#)

9



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[Report broken media](#)Score: **20.2%**

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| 88 | ✓ |
| 89 | ✗ |



A 64-year-old woman is referred by her GP to the haematology clinic with an incidental lymphocytosis noted first four months prior. On questioning, she reports that she has been feeling more fatigued over the past few months and has begun to experience episodes of early satiety, both of which she attributed to looking after her two grandchildren. She is otherwise well and denies any fevers, night sweats or unusual bruising.

On examination, she is slim with an unremarkable cardiovascular and respiratory exam. There is a fullness in the left upper quadrant which moves with inspiration but no lymphadenopathy.

Her blood tests are shown below:

Hb	140 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$200 \times 10^9/L$	(150 - 400)
WBC	$30.1 \times 10^9/L$	(4.0 - 11.0)
Neuts	$4.0 \times 10^9/L$	(2.0 - 7.0)
Lymphs	$25.0 \times 10^9/L$	(1.0 - 3.5)
Mono	$0.8 \times 10^9/L$	(0.2 - 0.8)
Eosin	$0.3 \times 10^9/L$	(0.0 - 0.4)
Blood Film	lymphocytosis with smudge cells	

Ultrasound abdomen confirms splenomegaly.

Chromosomal analysis is performed to guide further management.

Given the likely diagnosis, which of the following chromosomal findings would suggest a poor prognosis?

- ☐ >2% mutation immunoglobulin heavy chain variable region ×
- ☐ Deletion of 13q ×
- ☐ Deletion of 17p ×
- ☐ < 20% CD38 expression ×
- ☐ TP53 - wild-type ×

Submit answer

Reference ranges 

Score: **18%**

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Lymphs	$25.0 \times 10^9/L$	(1.0 - 3.5)
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Eosin	$0.3 \times 10^9/L$	(0.0 - 0.4)
Blood Film	lymphocytosis with smudge cells	

Ultrasound abdomen confirms splenomegaly.

Chromosomal analysis is performed to guide further management.

Given the likely diagnosis, which of the following chromosomal findings would suggest a poor prognosis?

>2% mutation immunoglobulin heavy chain variable region	2%
Deletion of 13q	12%
Deletion of 17p	76%
< 20% CD38 expression	2%
TP53 - wild-type	7%

del 17p is associated with a poor prognosis in CLL

Important for me Less important

This patient has chronic lymphocytic leukaemia (CLL) demonstrated by a history of significant lymphocytosis for > 3 months and splenomegaly with a blood film showing smudge cells. A bone marrow aspirate is not required in all CLL patients but may be indicated in patients with anaemia and/thrombocytopenia to confirm whether these may be attributed to marrow infiltration or splenic destruction.

The deletion of 17p is associated with a poor prognosis in CLL. All other options are markers of good prognosis. Note that a wild type TP53 refers to an unmutated form, however, a mutated TP53 is, by contrast, a bad prognostic marker.



Discuss (5)

Improve

Next question >

Chronic lymphocytic leukaemia: prognostic factors ★

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive
- TP53 mutation

Chromosomal changes

- deletion of the long arm of chromosome 13 (del 13q) is the most common abnormality, being seen in around 50% of patients. It is associated with a **good** prognosis
- deletions of part of the short arm of chromosome 17 (del 17p) are seen in around 5-10% of patients and are associated with a **poor** prognosis



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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

 2  0

[2012 CLL guidelines](#)

[Suggest link](#)


[Report broken link](#)

Media




[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)


Medicosis Perfectionalis - YouTube


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Score: **20.2%**


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| 89 | ✗ |



Question 53 of 89



A 54-year-old alcoholic man with chronic hepatitis C is taken to the emergency department by the police. There it was noted that the man had blisters and crusted lesions on his face and lower arms.

Laboratory tests showed elevated plasma porphyrins and elevated uroporphyrin I in the urine, and isocoproporphyrin in the faeces. Biopsy of the skin lesion showed subepidermal blisters with minimal inflammation, marked solar elastosis, thickening of the vessel wall in the papillary dermis and 'caterpillar bodies' in the roof of the blister.

Which of the following is the most likely diagnosis?

- | | |
|--|---|
| <input type="radio"/> Acute intermittent porphyria | × |
| <input type="radio"/> Delta-aminolevulinic acid dehydrase deficiency | × |
| <input type="radio"/> Erythropoietic protoporphyria | × |
| <input type="radio"/> Hereditary coproporphyria | × |
| <input type="radio"/> Porphyria cutanea tarda | × |

Submit answer

Reference ranges 

Score: **18%**

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44	✓
45	✗

46	✗
47	✗
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49	✓
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51	-
52	-
53	-



Question 53 of 89



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Which of the following is the most likely diagnosis?

Acute intermittent porphyria	8%
Delta-aminolevulinic acid dehydrase deficiency	2%
Erythropoietic protoporphyria	5%
Hereditary coproporphyria	6%
Porphyria cutanea tarda	79%

Porphyria cutanea tarda causes chronic blistering and crusting skin lesions on sun-exposed skin. Precipitating factors: iron (even if normal amounts), oestrogen and alcohol use, and chronic hepatitis C infection.

The findings on skin biopsy can help with the diagnosis but are not very specific (the 'caterpillar bodies' are essentially clumps of basement membrane material). The key to the diagnosis is the presentation and porphyrin analysis.



Discuss (4)

Improve

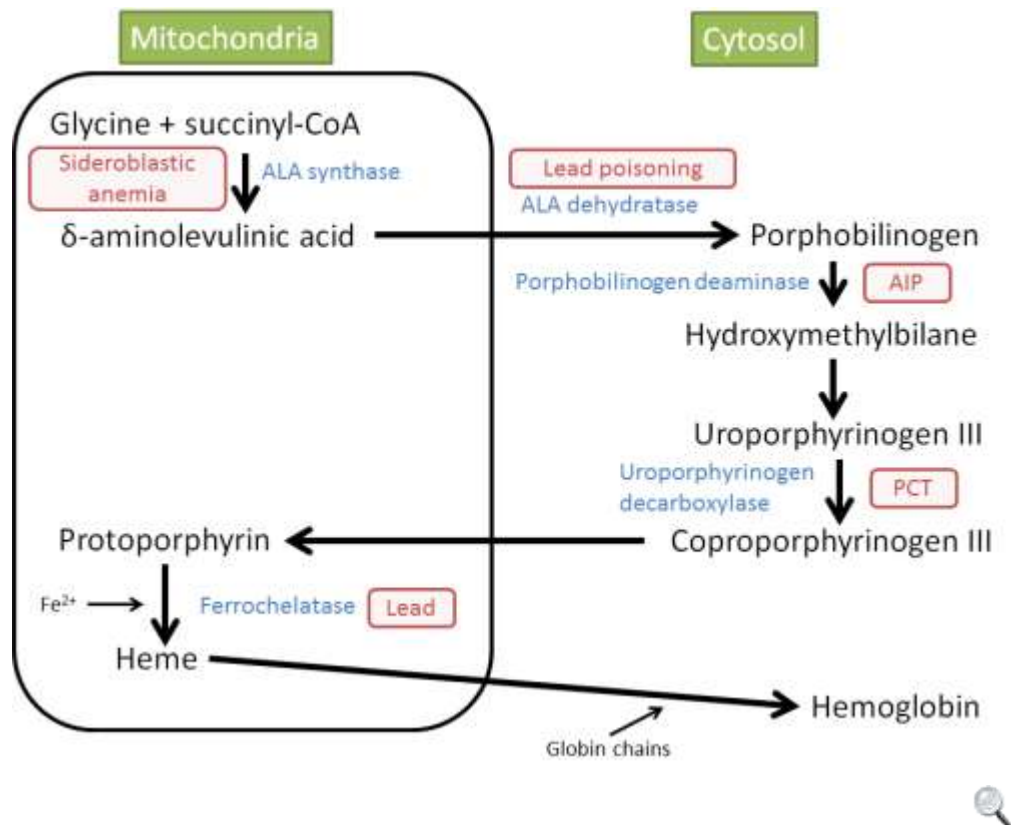
[Next question >](#)

Porphyrias ★

Overview

- abnormality in enzymes responsible for the biosynthesis of haem
- results in overproduction of intermediate compounds (porphyrins)

- may be acute or non-acute



Acute intermittent porphyria (AIP)




- autosomal dominant
- defect in porphobilinogen deaminase
- female and 20-40 year olds more likely to be affected
- typically present with abdominal symptoms, neuropsychiatric symptoms
- hypertension and tachycardia common
- urine turns deep red on standing

Porphyria cutanea tarda (PCT)

- most common hepatic porphyria
- defect in uroporphyrinogen decarboxylase
- may be caused by hepatocyte damage e.g. alcohol, oestrogens
- classically photosensitive rash with bullae, skin fragility on face and dorsal aspect of hands
- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp
- manage with chloroquine

Variegate porphyria

- autosomal dominant
- defect in protoporphyrinogen oxidase
- photosensitive blistering rash
- abdominal and neurological symptoms
- more common in South Africans

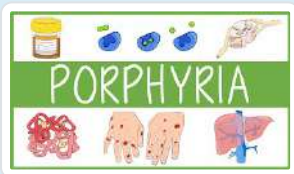
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Textbooks



High-yield textbook

Extended textbook

Media





Porphyria

Townsend Teaching - YouTube  5  0





Acute intermittent porphyria

Osmosis - YouTube  0  0

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| 87 | ✗ |
| 88 | ✓ |
| 89 | ✗ |



Question 54 of 89



A 68-year-old female, presents with lethargy and anorexia. She underwent a partial gastrectomy 3 years ago for bleeding gastric ulcer. Her blood results showed:

Hb	90 g/l
MCV	109 fL
Platelets	$60 \times 10^9/l$
WBC	$3.5 \times 10^9/l$
Blood film	Oval erythrocytes, macrocytic erythrocytes, hypersegmented neutrophils, low platelets and basophilic stippling

What is the underlying diagnosis?

- ☐ Sideroblast anaemia ×
- ☐ Spur cell haemolysis ×
- ☐ Vitamin-B12 deficiency ×
- ☐ Thalassaemia ×
- ☐ Myelodysplasia ×

Submit answer

Reference ranges 

Score: **18%**

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Question 54 of 89



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MCV	109 fL
Platelets	$60 \times 10^9/l$
WBC	$3.5 \times 10^9/l$
Blood film	Oval erythrocytes, macrocytic erythrocytes, hypersegmented neutrophils, low platelets and basophilic stippling

What is the underlying diagnosis?

Sideroblast anaemia	16%
Spur cell haemolysis	1%
Vitamin-B12 deficiency	70%
Thalassaemia	2%
Myelodysplasia	11%

Gastrectomy is defined as partial when a part of the stomach is removed surgically and as total when the entire stomach is removed. Typical indications are gastric cancer, recurrent gastric ulcers, large duodenal perforations, bleeding gastric ulcers and gastrointestinal stromal tumours. Malnutrition is less common after partial than after total gastrectomy, but the key nutritional deficiencies are iron-deficiency anaemia, calcium deficiency, and vitamin B12 deficiency. However, the hypersegmented neutrophils are strongly suggestive of B12 deficiency.

Hypersegmented neutrophils are hallmarks of B12 deficiency in multiple choice questions.




 Discuss (11)

 Improve

Next question >

Macrocytic anaemia ★

Macrocytic anaemia can be divided into causes associated with a megaloblastic bone marrow and those with a normoblastic bone marrow

Megaloblastic causes of macrocytic anaemia

- vitamin B12 deficiency
- folate deficiency
- e.g. secondary to methotrexate

Normoblastic causes of macrocytic anaemia

- alcohol
- liver disease
- hypothyroidism
- pregnancy
- reticulocytosis
- myelodysplasia
- drugs: cytotoxics



123



Next question >

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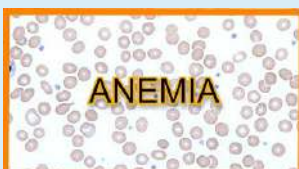


Textbooks

High-yield textbook

Extended textbook

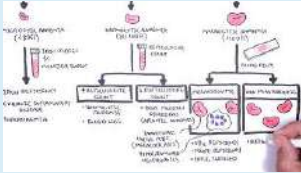
Media



[Anemia \(Types, Lab Findings, High Yield Images\)](#)

DirtyUSMLE - YouTube

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Anaemia (anemia) - classification (microcytic, normocytic and macrocytic) and pathophysiology

Armando Hasudungan - YouTube

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Score: **20.2%**

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84	✗
85	✗
86	✗
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88	✓
89	✗



A 19-year-old man is referred to see you as he has been suffering from recurrent epistaxis and he tells you that if he accidentally injures himself the wound bleeds for a long time.

Initial blood tests are as follows:

Hb	101 g/l
MCV	79 fl
Platelets	$298 \times 10^9/l$
WBC	$9.2 \times 10^9/l$
Bleeding time	Prolonged
PT	14 seconds
APTT	28 seconds
LDH	290 u/l (240 - 480 u/L)
Factor VIIIc	low
Ristocetin platelet aggregation test	Impaired aggregation

What is the single most likely diagnosis?

- ☐ Haemophilia A ×
- ☐ Haemophilia B ×
- ☐ Haemophilia C ×
- ☐ Idiopathic Thrombocytopenic Purpura (ITP) ×
- ☐ von Willebrand's disease ×

Submit answer

Reference ranges 

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A 19-year-old man is referred to see you as he has been suffering from recurrent epistaxis and he tells you that if he accidentally injures himself the wound bleeds for a long time.

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Factor VIIIc	low
Ristocetin platelet aggregation test	Impaired aggregation

What is the single most likely diagnosis?

Haemophilia A	26%
Haemophilia B	5%
Haemophilia C	2%
Idiopathic Thrombocytopenic Purpura (ITP)	1%
von Willebrand's disease	66%

This patient has a coagulopathy and normal platelets, which immediately excludes ITP. Factor VIIIc is low, meaning that the diagnosis must either be haemophilia A or von Willebrand's disease. In this patient two things favour the diagnosis of von Willebrand's over haemophilia A. Firstly, the bleeding time is prolonged and secondly, the platelet aggregation is impaired in response to ristocetin. Both of these would be normal in haemophilia.

Von Willebrand's disease ★

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemarthroses and muscle haematomas are rare

Role of von Willebrand factor

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types

- type 1: partial reduction in vWF (80% of patients)
- type 2*: abnormal form of vWF
- type 3**: total lack of vWF (autosomal recessive)

Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management

- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 2A VWD is caused by defective platelet adhesion due to decreased high molecular weight VWF multimers (i.e. the VWF protein is too small). Type 2B is characterised by a pathological increase of VWF-platelet interaction. Type 2M is caused by a decrease in VWF-platelet interaction (not related to loss of high molecular weight multimers). Type 2N is caused by abnormal binding of the VWF to Factor VIII. There is no clear correlation between symptomatic presentation and type of VWD however common themes amongst patients include excessive mucocutaneous bleeding, bruising in the absence of trauma and menorrhagia in females.

**type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease



123

[Next question >](#)**B***I***A****T**

Textbooks

[High-yield textbook](#)[Extended textbook](#)

Links

[British Committee for Standards in Haematology](#)

0 1

[2014 Von Willebrand's disease guidelines](#)[Suggest link](#)[Report broken link](#)

Media

Von Willebrand Disease Classification			
Type	Defect	Mechanism	Clinical Manifestations
Type 1	Quantitative defect	Quantitative decrease	Mild bleeding tendency
Type 2	Qualitative defect	Qualitative decrease	Mild to moderate bleeding tendency
Type 3	Quantitative defect	Quantitative decrease	Severe bleeding tendency

[Von Willebrand Disease and Qualitative Platelet Disorders](#)[Strong Medicine - YouTube](#)

3 0

Antithrombotic Medications
Inhibition of factor

- Antithrombotic medications include:
 - Anticoagulants (heparin, warfarin)
 - Thrombolytics (alteplase, streptokinase)
- They act by inhibiting the activation of factor X
- Anticoagulants are used to prevent thrombosis

[Prothrombotic Medications](#)[Strong Medicine - YouTube](#)

2 1



Von Willebrand disease

Osmosis - YouTube



2



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[Report broken media](#)

Score: **20.2%**

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Question 56 of 89



A 21-year-old girl complains of easy bruising. She has menorrhagia for which she is being investigated by the gynaecology team. She takes no regular medications. Her father had prolonged bleeding after a tooth extraction.

Blood tests show:

Hb	110 g/L
MCV	74 fL
WBC	$4.2 \times 10^9/L$
Platelets	$135 \times 10^9/L$
APTT	45 seconds
INR	1.0

What is the most likely diagnosis?

- ☐ Haemophilia B ×
- ☐ Anti-thrombin III deficiency ×
- ☐ Von Willebrand's disease ×
- ☐ Immune thrombocytopenia ×
- ☐ Haemophilia A carrier ×

Submit answer

Reference ranges 

Score: **18%**

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9	✓
10	×
11	✓
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Blood tests show:

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MCV	74 fL
WBC	$4.2 \times 10^9/L$
Platelets	$135 \times 10^9/L$
APTT	45 seconds
INR	1.0

What is the most likely diagnosis?

Haemophilia B

9%

Anti-thrombin III deficiency

3%

Von Willebrand's disease

78%

Immune thrombocytopenia

2%

Haemophilia A carrier

7%

Von-Willebrand's disease is an autosomal dominant condition (chromosome 12) that leads to a mild-moderate bleeding tendency. The prevalence of clinically significant cases is 1 in 10,000. Factor VIII is bound to vWF, which protects it from breakdown, so deficiency of vWF can lead to low factor VIII levels and a prolonged APTT. In this case the patient also has a microcytic anaemia, which would be in keeping with iron deficiency anaemia secondary to menorrhagia. Haemophilia B (Factor IX deficiency) is X-linked so does not affect females. Haemophilia A (Factor VIII deficiency) is also X-linked. Most carriers are asymptomatic. The APTT is normal in ITP. Anti thrombin III deficiency is a pro thrombotic condition.



Discuss (6)

Improve

Von Willebrand's disease ★

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemarthroses and muscle haematomas are rare

Role of von Willebrand factor

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
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- type 1: partial reduction in vWF (80% of patients)
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123

[Next question >](#)**B***I***A****T**

Textbooks

[High-yield textbook](#)[Extended textbook](#)

Links

[British Committee for Standards in Haematology](#)

0 1

[2014 Von Willebrand's disease guidelines](#)[Suggest link](#)[Report broken link](#)

Media

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[Von Willebrand Disease and Qualitative Platelet Disorders](#)[Strong Medicine - YouTube](#)

3 0

Antithrombotic Medications
Inhibition of factor

- Antithrombotic medications include:
 - Anticoagulants (heparin, warfarin)
 - Thrombolytics (alteplase, streptokinase)
- They act by inhibiting the activation of factors in the coagulation cascade
- Anticoagulants are used to prevent thrombosis

[Prothrombotic Medications](#)[Strong Medicine - YouTube](#)

2 1



Von Willebrand disease

Osmosis - YouTube



2



1

[Report broken media](#)

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| 85 | ✗ |
| 86 | ✗ |
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Question 57 of 89



A 72-year-old woman with breast cancer presents with a swollen, painful left calf. She is known to have metastases in the vertebral bodies and is taking denosumab as prophylaxis. A Doppler ultrasound is arranged which shows a proximal deep vein thrombosis on the left side. This is her first episode of venous thromboembolism. What is the most appropriate management?

- ☐ Warfarin for 3 months ×
- ☐ Warfarin for 6 months ×
- ☐ Low-molecular weight heparin for 3-6 months ×
- ☐ Direct oral anticoagulants (DOACs) for 3-6 months ×
- ☐ Aspirin 300 mg for 3 months ×

Submit answer

Reference ranges 

Score: **18%**

- 1 ×
- 2 ×
- 3 ×
- 4 ×
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Warfarin for 3 months	2%
Warfarin for 6 months	3%
Low-molecular weight heparin for 3-6 months	7%
Direct oral anticoagulants (DOACs) for 3-6 months	88%
Aspirin 300 mg for 3 months	0%

Cancer patients with VTE - 6 months of a DOAC

Important for me Less important



Discuss (3)
Improve

Next question >

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

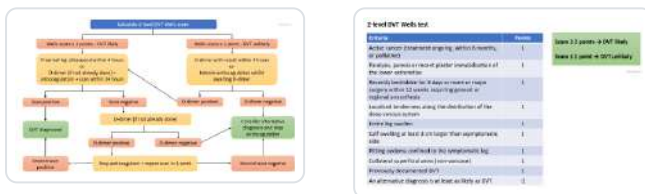
- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)
 - interim therapeutic anticoagulation used to mean giving low-molecular weight heparin
 - NICE updated their guidance in 2020. They now recommend using an anticoagulant that can be continued if the result is positive.
 - this means normally a direct oral anticoagulant (DOAC) such as apixaban or rivaroxaban
- if the scan is negative but the D-dimer is positive:
 - stop interim therapeutic anticoagulation
 - offer a repeat proximal leg vein ultrasound scan 6 to 8 days later

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test
 - this should be done within 4 hours. If not, interim therapeutic anticoagulation should be given until the result is available
 - if the result is negative then DVT is unlikely and alternative diagnoses should be considered
 - if the result is positive then a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if a proximal leg vein ultrasound scan cannot be carried out within 4 hours interim therapeutic anticoagulation should be administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

D-dimer tests

- NICE recommend either a point-of-care (finger prick) or laboratory-based test
- age-adjusted cut-offs should be used for patients > 50 years old



Management

The cornerstone of VTE management is anticoagulant therapy. This was historically done with warfarin, often preceded by heparin until the INR was stable. However, the development of DOACs, and an evidence base supporting their efficacy, has changed modern management.

Choice of anticoagulant

- the big change in the 2020 guidelines was the increased use of DOACs
- apixaban or rivaroxaban (both DOACs) should be offered first-line following the diagnosis of a DVT
 - instead of using low-molecular weight heparin (LMWH) until the diagnosis is confirmed, NICE now advocate using a DOAC once a diagnosis is suspected, with this continued if the diagnosis is confirmed
 - if neither apixaban or rivaroxaban are suitable then either LMWH followed by dabigatran or edoxaban OR LMWH followed by a vitamin K antagonist (VKA, i.e. warfarin)
- if the patient has active cancer
 - previously LMWH was recommended
 - the new guidelines now recommend using a DOAC, unless this is contraindicated
- if renal impairment is severe (e.g. < 15/min) then LMWH, unfractionated heparin or LMWH followed by a VKA

- if the patient has antiphospholipid syndrome (specifically 'triple positive' in the guidance) then LMWH followed by a VKA should be used

Length of anticoagulation

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer at increased risk
 - an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



123



Next question >

B

I



A



T



Textbooks

High-yield textbook

Extended textbook

Links

NICE

 5  0

2020 Venous thromboembolism guidelines

[Suggest link](#)

[Report broken link](#)

Media



[Deep vein thrombosis](#)



Osmosis - YouTube

 3  0



[Understanding Deep Vein Thrombosis \(DVT\)](#)



Zero To Finals - YouTube

 2  1




[Deep Vein Thrombosis - Overview \(pathophysiology, treatment, complications\)](#)


Armando Hasudungan - YouTube


 3  2


[Report broken media](#)


Score: **20.2%**


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Question 58 of 89



A 23-year-old gentleman reviewed by the on-call medical team after having become unwell in the radiology department. He was undergoing a contrast-enhanced MRI of the small bowel to investigate ongoing diarrhoea. He has no other past medical history and takes no regular medications. He is not known to have any allergies.

Ten minutes ago he started feeling his throat closing up and became very anxious. This was shortly after having been given a contrast agent by IV injection. The medical emergency team arrives quickly and note him to be tachycardia at 132/min and hypotensive with a blood pressure of 82/35mmHg. He also has a widespread erythematous rash over his body and feels itchy. He is treated for anaphylactic shock.

Which blood tests could confirm anaphylaxis?

- ☐ Histamine levels ×
- ☐ Mast cell tryptase immediately and repeat within one to two hours ×
- ☐ Mast cell tryptase immediately and repeat within 12 hours ×
- ☐ Mast cell tryptase immediately and repeat within 24 hours ×
- ☐ Serum immunoglobulins ×

Submit answer

Reference ranges 

Score: **18%**

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Which blood tests could confirm anaphylaxis?




Histamine levels	1%
Mast cell tryptase immediately and repeat within one to two hours	50%
Mast cell tryptase immediately and repeat within 12 hours	36%
Mast cell tryptase immediately and repeat within 24 hours	12%
Serum immunoglobulins	1%

Anaphylaxis - serum tryptase levels rise following an acute episode

Important for me

Less important

The correct answer is mast cell tryptase immediately and repeat within one to two hours. Tryptase levels are the most specific marker for an anaphylactic reaction. Tryptase is a marker of mast cell activation. Serum concentration is normally very low and will quickly return to normal, which is why an immediate sample can be useful but should never delay treatment. Tryptase levels increase to maximum levels over 30 minutes from the onset of symptoms, then peaks at one to two hours. The half-life of tryptase is roughly two hours and may return to normal within six to eight hours. This means that a sample at 12 or 24 hours may not confirm anaphylaxis. Histamine levels can be elevated in various conditions, including simple allergic reactions and does not help to distinguish anaphylaxis. Immunoglobulins are elevated in cell-mediated immune responses.

		 Discuss (4)	Improve
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Next question >

Anaphylaxis ★

Anaphylaxis may be defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction.

Common identified causes of anaphylaxis:

- food (e.g. nuts) - the most common cause in children
- drugs
- venom (e.g. wasp sting)

Features

The Resus Council UK define anaphylaxis as:

- the sudden onset and rapid progression of symptoms
- **A**irway and/or **B**reathing and/or **C**irculation problems
- **A**irway problems may include:
 - swelling of the throat and tongue → hoarse voice and stridor
- **B**reathing problems may include:
 - respiratory wheeze
 - dyspnoea
- **C**irculation problems may include:
 - hypotension
 - tachycardia

This means that if there are no ABC problems then the patient is technically not having anaphylaxis.

Around 80-90% of patients also have skin and mucosal changes:

- generalised pruritus
- widespread erythematous or urticarial rash

Management

Anaphylaxis is one of the few times when you would not have time to look up the dose of a

medication. The Resuscitation Council guidelines on anaphylaxis have recently been updated. **Intramuscular adrenaline** is by far the most important drug in anaphylaxis and should be given as soon as possible. Previously IV hydrocortisone was also recommended but the evidence base for this was poor and it was removed in the 2021 update.

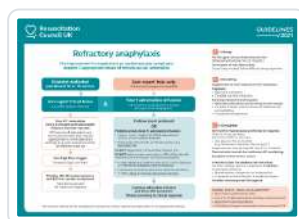
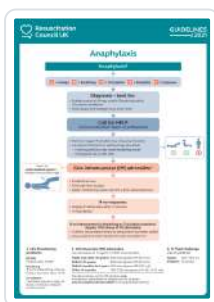
The recommended doses for adrenaline are as follows: **BNF**

Age	Adrenaline dose
< 6 months	100 - 150 micrograms (0.1 - 0.15 ml 1 in 1,000)
6 months - 6 years	150 micrograms (0.15 ml 1 in 1,000)
6-12 years	300 micrograms (0.3ml 1 in 1,000)
Adult and child > 12 years	500 micrograms (0.5ml 1 in 1,000)

Adrenaline can be repeated every 5 minutes if necessary. The best site for IM injection is the anterolateral aspect of the middle third of the thigh.

Refractory anaphylaxis

- defined as respiratory and/or cardiovascular problems persist despite 2 doses of IM adrenaline
- IV fluids should be given for shock
- expert help should be sought for consideration of an IV adrenaline infusion



Management following stabilisation:

- non-sedating oral antihistamines, in preference to chlorphenamine, may be given following initial stabilisation especially in patients with persisting skin symptoms (urticaria and/or angioedema)
- sometimes it can be difficult to establish whether a patient had a true episode of anaphylaxis. Serum **tryptase** levels are sometimes taken in such patients as they remain elevated for up to 12 hours following an acute episode of anaphylaxis
- all patients with a new diagnosis of anaphylaxis should be referred to a specialist allergy clinic
- an adrenaline injector should be given as an interim measure before the specialist allergy assessment (unless the reaction was drug-induced)
 - patients should be prescribed 2 adrenaline auto-injectors
 - training should be provided on how to use it

- a risk-stratified approach to discharge should be taken as biphasic reactions can occur in up to 20% of patients

The Resus Council UK recommend the following risk-stratified approach to discharge:

- fast-track discharge (after 2 hours of symptom resolution):
 - good response to a single dose of adrenaline
 - complete resolution of symptoms
 - has been given an adrenaline auto-injector and trained how to use it
 - adequate supervision following discharge
- minimum 6 hours after symptom resolution
 - 2 doses of IM adrenaline needed, or
 - previous biphasic reaction
- minimum 12 hours after symptom resolution
 - severe reaction requiring > 2 doses of IM adrenaline
 - patient has severe asthma
 - possibility of an ongoing reaction (e.g. slow-release medication)
 - patient presents late at night
 - patient in areas where access to emergency access care may be difficult
 - observation for at 12 hours following symptom resolution



123



Next question >

B

I



A



Textbooks

High-yield textbook

Extended textbook

Links

Clinical Knowledge Summaries

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
[Angio-oedema and anaphylaxis](#)

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Osmosis - YouTube  1  1

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A 43 year old man is brought to the Emergency Department by his wife. She has become worried about him in the past six months as he has become increasingly confused, aggressive and depressed. He has also lost 4kg in weight in this time and has developed severe, intermittent abdominal pain and diarrhoea, and complains of constant headaches.

Examination reveals a normal cardiorespiratory examination but the abdomen is diffusely tender and there is tender fullness in the right upper quadrant. Neurological examination reveals minor hypotonia throughout and there are bilateral radial nerve palsies as well as a left common peroneal nerve palsy. Sensation appears intact. He is alert but confused with an abbreviated mental test score of 7/10.

Blood tests reveal:

Sodium	136mmol/L	ALP	135U/L	Haemoglobin	79g/L
Potassium	5.1mmol/L	AST	265U/L	MCV	101fL
Urea	7.1mmol/L	ALT	298U/L	White cells	$9.4 \times 10^9/L$
Creatinine	102 μ mol/L	GGT	197U/L	Neutrophils	$5.6 \times 10^9/L$
CRP	10mg/L	Bilirubin	12 μ mol/L	Lymphocytes	$3.1 \times 10^9/L$
Calcium (corr)	2.34mmol/L			Eosinophils	$0.1 \times 10^9/L$
Phosphate	0.56mmol/L			Basophils	$0.6 \times 10^9/L$
Magnesium	0.76mmol/L				
Glucose	3.8mmol/L				

The blood film shows anaemia with a dimorphic picture, significant reticulocytosis and high basophil numbers with cytoplasmic stippling.

The patients wife tells you all the symptoms coincided with the patient starting a new job as a loading crane driver at a scrap-yard.

What is the most likely diagnosis?

- ☐ Chronic alcoholism ×
- ☐ Acute promyelocytic leukaemia ×
- ☐ Porphyria cutanea tarda ×

☐ Chronic lead poisoning



☐ Minimata disease



Submit answer

Reference ranges ▾

Score: **18%**

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Glucose	3.8mmol/L				

The blood film shows anaemia with a dimorphic picture, significant reticulocytosis and high basophil numbers with cytoplasmic stippling.

The patients wife tells you all the symptoms coincided with the patient starting a new job as a loading crane driver at a scrap-yard.

What is the most likely diagnosis?

Chronic alcoholism	2%
Acute promyelocytic leukaemia	2%
Porphyria cutanea tarda	8%

Abdominal pain, constipation, neuropsychiatric features, basophilic stippling → lead poisoning

Important for me Less important

The above vignette gives a classical description of chronic lead poisoning, also known as plumbism or Devon colic. The typical signs are gastrointestinal and neuropsychiatric and include severe, colicky abdominal pain with weight loss and diarrhoea and a metallic taste in the mouth. Insidious neurological signs include headache, difficulty concentrating, subtle personality changes including aggression and difficulty sleeping, dyspraxia and cerebellar signs. The pathognomonic hallmark of chronic lead poisoning is a radial nerve palsy, or wrist drop, although many peripheral nerve palsies may be seen. Patients may also have a bluish discolouration to their skin and a blue line on the gums, known as Burton's line, is very rarely seen. Biochemically, a hepatitic picture can be seen and also occasionally renal impairment due to proximal renal tubular failure, particularly with increased excretion of phosphate and glucose and acidification of the urine. However, most notable is the haematological impact of lead poisoning with a pronounced anaemia, often with dimorphic picture and reticulocytosis due to arrest of the haem biosynthetic pathway. Basophilia with stippling is seen and bone marrow trephine may show ring sideroblasts.

Blood lead levels do not correlate well with total lead burden and the diagnosis may be missed due to incorrect assay or test selection. Since lead is concentrated in red cells, whole blood levels of lead rather than plasma must be analysed, however testing for enzymes affected by lead is more reliable than whole lead levels alone, and hence erythrocyte zinc protoporphyrin (ZPP) levels and delta aminolevulinic acid dehydratase (ALAD) are more reliable. These, coupled with skeletal analysis and blood lead levels are used to test for occupational lead poisoning. The term metal fume fever is used to describe many syndromes of heavy metal and metal oxide poisonings, often in gantry crane drivers who deposit scrap metals in furnaces from above. Many scrap metals are coated in lead based paints leading to occupational lead toxicity syndromes.

Lead poisoning is clinically similar to porphyria and pathologically an interruption in haem pathways are seen in both. The classical hallmark of porphyria cutanea tarda is a blistering photosensitive rash that is not present in this case. Chronic alcoholism may cause B12 deficiency and hence a megaloblastic anaemia and confusion but it is unlikely to cause this constellation of neuropathies and does not explain the basophilic stippling. There is no mention of the patient's alcohol habits either. An acute promyelocytic leukaemia presents with non specific symptoms and infections. It may present with sudden onset neurological symptoms only if there is a spontaneous intracranial bleed, in which case the outlook is bleak. It is unlikely here. Minimata disease is an acute mercury toxicity and presents with neuropsychiatric symptoms and rapid death. It would not be expected to cause the haematological picture seen here.

[Discuss \(11\)](#)[Improve](#)[Next question >](#)

Lead poisoning ★

Along with acute intermittent porphyria, lead poisoning should be considered in questions giving a combination of abdominal pain and neurological signs. Lead poisoning results in defective ferrochelatase and ALA dehydratase function.

Features

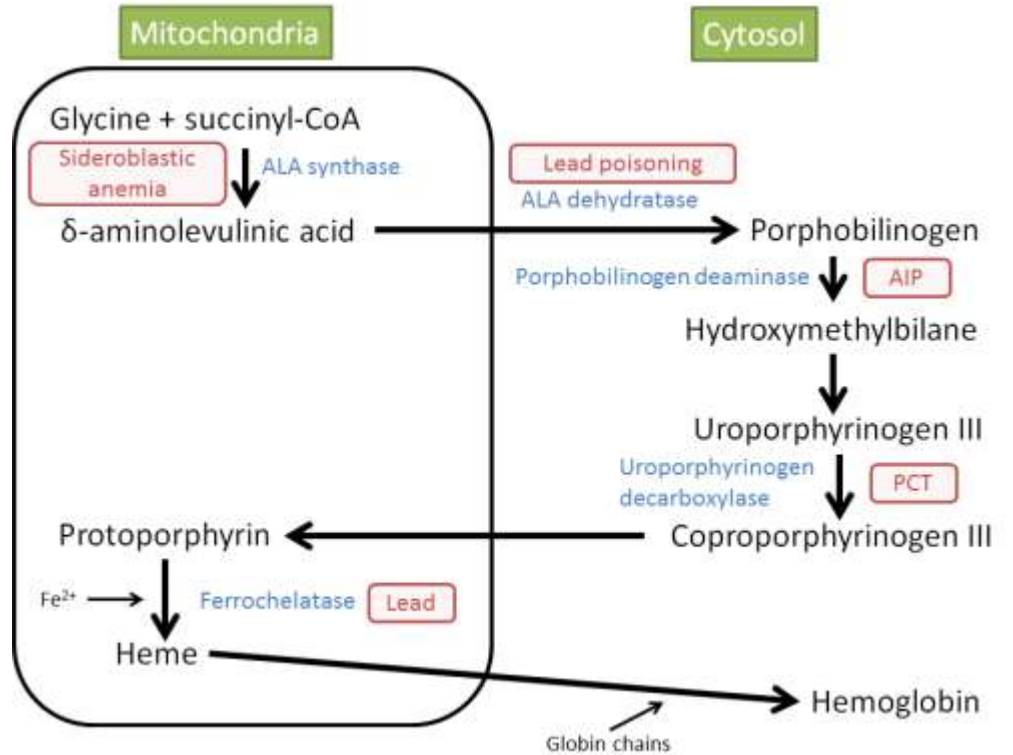
- abdominal pain
- peripheral neuropathy (mainly motor)
- neuropsychiatric features
- fatigue
- constipation
- blue lines on gum margin (only 20% of adult patients, very rare in children)

Investigations

- the blood lead level is usually used for diagnosis. Levels greater than 10 mcg/dl are considered significant
- full blood count: microcytic anaemia. Blood film shows red cell abnormalities including basophilic stippling and clover-leaf morphology
- raised serum and urine levels of delta aminolaevulinic acid may be seen making it sometimes difficult to differentiate from acute intermittent porphyria
- urinary coproporphyrin is also increased (urinary porphobilinogen and uroporphyrin levels are normal to slightly increased)
- in children, lead can accumulate in the metaphysis of the bones although x-rays are not part of the standard work-up

Management - various chelating agents are currently used:

- dimercaptosuccinic acid (DMSA)
- D-penicillamine
- EDTA
- dimercaprol



+

Q

123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Score: **20.2%**

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A 30-year-old man with acute myeloid leukaemia receives a bone marrow transplant from a matched unrelated donor.

7 days post-transplant, he develops a non-blanching purpuric rash over both legs. The rash is not itchy or scaly.

His heart rate 98/min and his blood pressure is 124/72 mmHg. His temperature is 37.3 °C and he is otherwise asymptomatic.

Blood tests are as follows:

Hb	89 g/l	Na ⁺	138 mmol/l
Platelets	9 * 10 ⁹ /l	K ⁺	3.2 mmol/l
WBC	0.8 * 10 ⁹ /l	Urea	4 mmol/l
Neuts	0.2 * 10 ⁹ /l	Creatinine	62 µmol/l
CRP	10 mg/l		

What is the most likely cause for the rash?

- ☐ Fungal infection ×
- ☐ Graft vs host disease ×
- ☐ Henoch Schonlein purpura ×
- ☐ Meningitis ×
- ☐ Thrombocytopenia ×

Submit answer

Reference ranges 

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Neuts	0.2 * 10 ⁹ /l	Creatinine	62 µmol/l
CRP	10 mg/l		

What is the most likely cause for the rash?

Fungal infection	2%
Graft vs host disease	57%
Henoch Schonlein purpura	7%
Meningitis	1%
Thrombocytopenia	33%



This man is on day 7 of his transplant and his blood counts are starting to drop, including his platelets. Thrombocytopenia typically causes small purpuric spots that are otherwise asymptomatic.

A fungal infection is possible in an immunosuppressed patient but would be more likely to cause an itchy or painful rash with a different appearance.

Graft vs host disease typical causes a dry scaly rash and develops when the patients immune system is starting to recover, around 2 weeks after transplant.

Henoch Schonlein purpura typically affects children and is associated with a glomerulonephritis. It is immune mediated so unlikely in someone who is still profoundly immunosuppressed.

Meningitis can cause a non-blanching purpuric rash but the patient would be symptomatic with headache, fever, meningism and a CRP rise.

   Discuss (6)  Improve

Next question >

Thrombocytopenia ★

Causes of severe thrombocytopenia

- ITP
- DIC
- TTP
- haematological malignancy






Causes of moderate thrombocytopenia

- heparin induced thrombocytopenia (HIT)
- drug-induced (e.g. quinine, diuretics, sulphonamides, aspirin, thiazides)
- alcohol
- liver disease
- hypersplenism
- viral infection (EBV, HIV, hepatitis)
- pregnancy
- SLE/antiphospholipid syndrome
- vitamin B12 deficiency

Pseudothrombocytopenia has been reported in association with the use of EDTA as an anticoagulant



Next question >

B *I*  **A** ▼    ▼ **T** ▼  ▼  

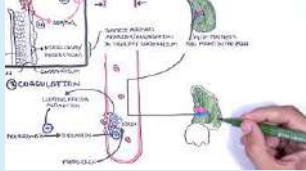
Textbooks

- High-yield textbook
- Extended textbook

High-yield textbook

Extended textbook

Media

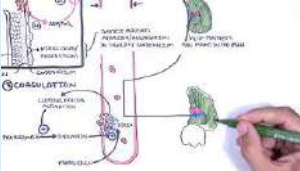


Thrombocytopenia (low platelets) Overview - platelet physiology, classification, pathophysiology

Armando Hasudungan - YouTube

👍 2 👎 0

Report broken media



Thrombocytopaenia (low platelets) Overview - platelet physiology, classification, pathophysiology

Armando Hasudungan - YouTube

👍 2 👎 0

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Score: **20.2%**

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A 45-year-old woman is admitted with chest pain three days after binge drinking 4 bottles of wine and 250mL of spirits.

She has a background of alcohol excess and systemic lupus erythematosus. She has a family history of G6PD deficiency on her father's side.

On examination, she is hemodynamically stable but jaundiced. She has pain on palpation over her right upper quadrant. Chest is clear and heart sounds are normal.

Hb	67 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$130 \times 10^9/L$	(150 - 400)
WBC	$9.8 \times 10^9/L$	(4.0 - 11.0)
Bilirubin	72 $\mu\text{mol/L}$	(3 - 17)
ALP	360 u/L	(30 - 100)
ALT	70 u/L	(3 - 40)
Amylase	67 u/L	(40-140)
Triglycerides	5.8 mmol/L	(<1.7)
LDH	1095 IU/L	(105-333)
Direct anti-globulin test	Negative	

Spur cells and acanthocytes are present on blood film.

Given the likely diagnosis, what treatment from the following options would be most appropriate?

<input type="radio"/> Abstinence from alcohol	×
<input type="radio"/> Ascorbic acid	×
<input type="radio"/> Intravenous fluids	×
<input type="radio"/> Liver transplantation	×
<input type="radio"/> Oral prednisolone	×

Submit answer

Score: **18%**

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LDH	1095 IU/L	(105-333)
Direct anti-globulin test	Negative	

Spur cells and acanthocytes are present on blood film.

Given the likely diagnosis, what treatment from the following options would be most appropriate?

Abstinence from alcohol	63%
Ascorbic acid	11%
Intravenous fluids	8%
Liver transplantation	2%
Oral prednisolone	16%

Zieve syndrome usually resolves with abstinence from alcohol

This patient is presenting with jaundice, hyper-triglyceridaemia, and Coomb's negative haemolytic anaemia due to alcoholism and recent binge. The diagnosis here is Zieve syndrome - a rare complication of alcohol excess that is thought to be caused by changes in the red cell membrane due to the transient hyperlipidaemia seen following alcohol binges.

Abstinence from alcohol is the correct answer. Treatment of Zieve syndrome is with supportive management with blood transfusion and abstinence from alcohol. In rare cases, plasmapheresis may be required.

Ascorbic acid is incorrect. This can be used in the treatment of G6PD deficiency, however, this patient does not have this condition. G6PD is inherited in an X-linked recessive pattern and so a female child of a male with G6PD deficiency would be a carrier. G6PD deficiency would also not explain the cholestatic liver function tests and rise in triglycerides.

Intravenous fluids is incorrect. IV fluids would be indicated if there was evidence of pancreatitis, or if the patient was hemodynamically unstable. In this case, the patient has severe anaemia, but in the context of haemodynamic stability IV fluids would be inappropriate as they would lead to a further drop in Hb concentration via a dilutional effect.

Liver transplantation is incorrect. The King's college criteria state that for non-paracetamol-induced liver injury an INR >6.5 or three from; bilirubin of greater than $600\mu\text{mol/L}$, an interval of >7 days between jaundice and encephalopathy, age <10 years or >40 , INR >3.5 , drug-induced or indeterminate cause of hepatitis, would be poor prognostic features and indicate liver transplant may be required.

Oral prednisolone is incorrect. This would be an option for alcoholic hepatitis or autoimmune haemolytic anaemia. In this case, the direct coomb's test is negative indicating that the low haemoglobin is not a result of immune-mediated haemolysis.



Discuss (1)

Improve

Next question >

Haemolytic anaemias: by cause ★

Hereditary haemolytic anaemias can be subdivided into membrane, metabolism or haemoglobin defects

Hereditary causes

- membrane: hereditary spherocytosis/elliptocytosis
- metabolism: G6PD deficiency
- haemoglobinopathies: sickle cell, thalassaemia

Acquired haemolytic anaemias can be subdivided into immune and non-immune causes

Acquired: immune causes (Coombs-positive)

- autoimmune: warm/cold antibody type
- alloimmune: transfusion reaction, haemolytic disease newborn
- drug: methyldopa, penicillin

Acquired: non-immune causes (Coombs-negative)

- microangiopathic haemolytic anaemia (MAHA): TTP/HUS, DIC, malignancy, pre-eclampsia
- prosthetic heart valves
- paroxysmal nocturnal haemoglobinuria
- infections: malaria
- drug: dapsone
- Zieve syndrome
 - rare clinical syndrome of Coombs-negative haemolysis, cholestatic jaundice, and transient hyperlipidaemia associated with heavy alcohol use, typically following a binge
 - typically resolves with abstinence from alcohol



123



Next question >

B

I



A



T



Textbooks

High-yield textbook

Extended textbook

Media



Score: **20.2%**

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A 52-year-old male was seen in the rapid access Transient Ischaemic Attack (TIA) clinic. He presented to his GP with new onset left leg and arm weakness three days ago. The weakness lasted for 90 minutes and fully resolved with no residual defect. He had a past medical history of hypertension, obstructive sleep apnoea and a left sided deep vein thrombosis eight years ago. His medication comprised ramipril 5mg OD. He smoked ten cigarettes per day and did not drink alcohol.

On examination, he had obvious truncal obesity and a flushed complexion. Blood pressure was 128/82 mmHg, heart rate 78/min, respiratory rate 16/min and oxygen saturations 99% on air. Cardiovascular examination revealed a regular pulse and nil else of note. Respiratory and gastrointestinal examination were normal, though examination of the abdomen was somewhat limited by the presence of truncal obesity. Neurological examination was unremarkable with normal cranial nerve, fundoscopy and peripheral neurological examinations.

Initial investigations revealed the following results:

Hb	191 g/l
MCV	98 fl
Hct	0.523
Platelets	502 * 10 ⁹ /l
WBC	14.0 * 10 ⁹ /l
Neutrophils	86%
Lymphocytes	10%
Monocytes	4%

HbA1c	43 mmol/mol
Fasting cholesterol	5.6 mmol/l

ECG: 76bpm normal sinus rhythm no other abnormality

Chest x-ray: unremarkable

24 hr ECG: no arrhythmia seen

Echo: normal systolic function, mild aortic stenosis with pressure gradient of 42mmHg

CT head: normal intracranial appearances, no evidence of mass shift, space occupying lesion or haemorrhage

What is the most appropriate next investigation most likely to lead to the underlying diagnosis?

- | | |
|--|---|
| <input type="radio"/> Cardiac catheterization | × |
| <input type="radio"/> Testing for presence of JAK2 mutation | × |
| <input type="radio"/> Bone marrow biopsy | × |
| <input type="radio"/> Radioisotope scanning of circulating blood volumes | × |
| <input type="radio"/> MRI scanning of the abdomen | × |

Submit answer

Reference ranges ▾

Score: **18%**

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| 6 | × |
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24 hr ECG: no arrhythmia seen



Echo: normal systolic function, mild aortic stenosis with pressure gradient of 42mmHg

CT head: normal intracranial appearances, no evidence of mass shift, space occupying lesion or haemorrhage

What is the most appropriate next investigation most likely to lead to the underlying diagnosis?

Cardiac catheterization	2%
Testing for presence of JAK2 mutation	93%
Bone marrow biopsy	3%
Radioisotope scanning of circulating blood volumes	1%
MRI scanning of the abdomen	1%

This gentleman has polycythaemia rubra vera (PRV). Whilst all of the above investigations may facilitate the diagnostic process, this question asks *What is the most appropriate next investigation most likely to lead to the underlying diagnosis?*. Testing for JAK2 mutation has widely surpassed the use of radioisotope scanning and is diagnostic of PRV. It is, therefore, the best option.



Discuss (5)
Improve

Next question >

Polycythaemia vera: features ★

Polycythaemia vera (previously called polycythaemia rubra vera) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with polycythaemia vera and this has resulted in significant changes to the diagnostic criteria. The incidence of polycythaemia vera peaks in the sixth decade.

Features

- pruritus, typically after a hot bath
- splenomegaly
- hypertension
- hyperviscosity
 - arterial thrombosis
 - venous thrombosis
- haemorrhage (secondary to abnormal platelet function)
- low ESR

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed

- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:

- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphatase

The diagnostic criteria for polycythaemia vera have recently been updated by the BCSH. This replaces the previous polycythaemia vera Study Group criteria.

JAK2-positive polycythaemia vera - diagnosis requires both criteria to be present

Criteria	Notes
A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

Criteria	Notes
A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly

Criteria	Notes
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count $>450 \times 10^9/l$)
B2	Neutrophil leucocytosis (neutrophil count $> 10 \times 10^9/l$ in non-smokers; $> 12.5 \times 10^9/l$ in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin

Next question >

B


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Textbooks

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Extended textbook

Links

Clinical Knowledge Summaries




1




3

Polycythaemia guidelines

British Committee for Standards in Haematology



5



2

2005 polycythaemia guidelines

Suggest link

Report broken link

Media



Polycythemia Vera

Medicosis Perfectionalis - YouTube

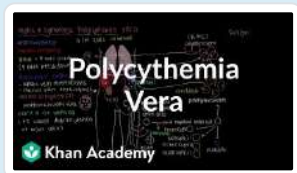
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Polycythemia vera

Osmosis - YouTube

👍 1 👎 0



What is polycythemia vera?

Khan Academy - YouTube

👍 0 👎 0



Polycythemia: Clinical Features, Management and Mnemonics

Townsend Teaching - YouTube

👍 2 👎 1

[Report broken media](#)

Score: **20.2%**

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An 18-year-old man presents to the emergency department with headache and discolouration of his face. He has a past medical history of NADH methaemoglobinaemia reductase deficiency. He does not smoke cigarettes or drink alcohol.

His observations are as follows: heart rate 94 beats per minute, oxygen saturations 85% on room air, blood pressure 120/77 mmHg, respiratory rate 20/minute and temperature 37°C.

Despite administration of 15L of oxygen via a non-rebreathe mask, the Sp2 remains 85%.

On examination, he appears cyanotic. The cardiorespiratory examination is unremarkable.

Plain radiography of the chest is normal.

ABG results:

pH	7.36	(7.35-7.45)
pO2	11 kPa	(11-13)
pCO2	4 kPa	(4-6)
Hb	136 g/L	(135-175)
Lactate	2.0 mmol/L	(0-2)
MetHb	30%	(0.2-0.6)

What is the most appropriate treatment?

☐ Antibiotic treatment
 ×

☐ Ascorbic acid
 ×

☐ Methylene blue
 ×

☐ No specific treatment
 ×

☐ Thrombolysis
 ×

Submit answer

Score: **18%**

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Hb	136 g/L	(135-175)
Lactate	2.0 mmol/L	(0-2)
MetHb	30%	(0.2-0.6)

What is the most appropriate treatment?

Antibiotic treatment	0%
Ascorbic acid	71%
Methylene blue	27%
No specific treatment	1%
Thrombolysis	0%

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency

Important for me Less important




Ascorbic acid is correct. This patient has NADH methaemoglobinaemia reductase deficiency, which is a congenital form of methaemoglobinaemia. IV methylene blue is ineffective in this form of the disease. He has evidence of a deterioration in his condition requiring treatment with a methaemoglobin level $\geq 30\%$, cyanosis, headache and a low peripheral oxygen saturation level despite normal arterial oxygen content. Ascorbic acid has been shown to be effective in the treatment of this disorder.

Methylene blue is incorrect. This is not effective in this form of methaemoglobinaemia but is the typical treatment for acquired causes.

Antibiotics treatment is incorrect. The patient is afebrile with a normal chest x-ray and there is no history of cough or shortness of breath. An infection seems unlikely.

No specific treatment is incorrect. Symptoms and a methaemoglobin level $\geq 30\%$ are both indications for treatment in this condition.

Thrombolysis is incorrect. While a pulmonary embolism is a plausible cause of low peripheral oxygen saturations with a normal examination and chest x-ray, the clinical context otherwise does not suggest this as the diagnosis. Furthermore, the typical indication for thrombolysis in pulmonary embolism is hypotension, which is absent in this case.

		 Discuss (10)	Improve
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Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO₂ but decreased oxygen saturation

Management

- NADH methaemoglobinemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Links

Life in the Fast Lane

6 3

[Methaemoglobinemia](#)

The Internet Book of Critical Care

10 4

[Methemoglobinemia](#)

[Suggest link](#)

[Report broken link](#)

Media



Methaemoglobinaemia

Osmosis - YouTube 7 2

[Report broken media](#)

Score: **20.2%**

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Question 64 of 89



A 34 year old man is admitted under the medics from the emergency department with central abdominal pain and vomiting not responding to IV morphine. He had been seen by the surgeons earlier in the day as an acute abdomen, but the CT scan they did of his abdomen and pelvis revealed no abnormalities, and his bloods suggested no surgical cause of the abdominal pain.

You note that the patient has presented to the emergency department five times in the past two years with similar problems, and no cause has ever been found, with the patient being discharged one or two days later with analgesia.

On examination his abdomen is generally tender with evidence of voluntary guarding. On further examination you note that he has a rash on the back of his hands, neck and cheeks. This rash consists of several small fluid filled bullae.

His past medical history includes depression - for which he is taking citalopram, and one short psychiatric inpatient stay for an episode of psychosis.

What is the most likely diagnosis?

- ☐ Erythropoietic protoporphyria ×
- ☐ Porphyria cutanea tarda ×
- ☐ Hereditary coproporphyria ×
- ☐ Acute intermittent porphyria ×
- ☐ Congenital erythropoietic porphyria ×

Submit answer

Reference ranges 

Score: **18%**

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His past medical history includes depression - for which he is taking citalopram, and one short psychiatric inpatient stay for an episode of psychosis.

What is the most likely diagnosis?

Erythropoietic protoporphyria	3%
Porphyria cutanea tarda	40%
Hereditary coproporphyria	6%
Acute intermittent porphyria	50%
Congenital erythropoietic porphyria	1%

The porphyrias are a group of rare inborn errors of metabolism caused by abnormalities of enzymes involved in the biosynthesis of haem, resulting in overproduction of intermediate compounds called porphyrins.

Three patterns of symptoms occur clinically with porphyrias:

- 1) Neurovisceral - neuropathy, epilepsy, psychiatric disorders, abdominal, vomiting, constipation
- 2) Photosensitive - bullous eruption in sun exposed areas
- 3) Haemolytic

Neurovisceral only	Photosensitive only	Mixed
Acute intermittent porphyria	Porphyria cutanea tarda	Variegate porphyria

Aminolaevulinic acid dehydrogenase porphyria	Congenital erythropoietic porphyria	Hereditary coproporphyria
-	Erythropoietic protoporphyria	-

This patient has both photosensitive symptoms; his rash, and neurovisceral symptoms; abdominal pain and previous psychiatric history. The only mixed presentation porphyria given as a possible answer is hereditary coproporphyria, hence it is the correct answer.

Ref: Kumar and Clark's Clinical medicine: Eight Edition Pages; 1043-1045

👍

👎

Discuss (8)

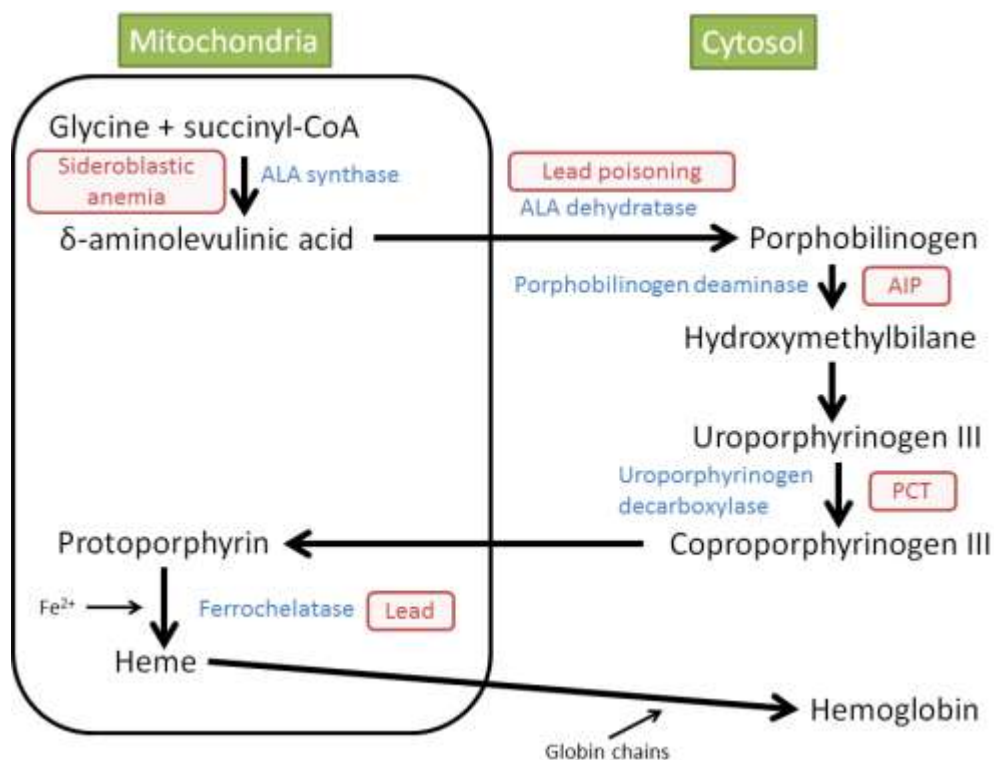
Improve

Next question >

Porphyrias ★

Overview

- abnormality in enzymes responsible for the biosynthesis of haem
- results in overproduction of intermediate compounds (porphyrins)
- may be acute or non-acute



Acute intermittent porphyria (AIP)

- autosomal dominant
- defect in porphobilinogen deaminase
- female and 20-40 year olds more likely to be affected

- typically present with abdominal symptoms, neuropsychiatric symptoms
- hypertension and tachycardia common
- urine turns deep red on standing

Porphyria cutanea tarda (PCT)

- most common hepatic porphyria
- defect in uroporphyrinogen decarboxylase
- may be caused by hepatocyte damage e.g. alcohol, oestrogens
- classically photosensitive rash with bullae, skin fragility on face and dorsal aspect of hands
- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp
- manage with chloroquine

Variegate porphyria

- autosomal dominant
- defect in protoporphyrinogen oxidase
- photosensitive blistering rash
- abdominal and neurological symptoms
- more common in South Africans



123



Next question >

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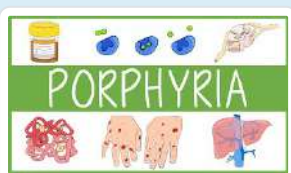


Textbooks



High-yield textbook

Extended textbook

Media





Porphyria

Townsend Teaching - YouTube  5  0



Acute intermittent porphyria

Osmosis - YouTube  0  0

[Report broken media](#)

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A 62 year old man is attending his GP as part of regular screening. He has a past medical history significant only for hypertension for which he has been taking amlodipine for many years. He reports no specific symptoms of note and is still working full time as an accountant. His blood pressure on this visit is 132/78mmHg and his urinalysis shows no abnormalities. Blood tests were taken for routine monitoring.

Hb	13.8 g/dl
Platelets	362 * 10 ⁹ /l
WBC	6.3 * 10 ⁹ /l

Na ⁺	142 mmol/l
K ⁺	4.2 mmol/l
Urea	4.6 mmol/l
Creatinine	84 µmol/l

Adjusted calcium	2.41mmol/l
Lactate Dehydrogenase	300 IU/l
Albumin	36 g/l
Globulin	52 g/l

An abnormal protein band is detected during analysis and the GP arranges for further review with the Haematologist at the hospital. Further investigations are undertaken:

Monoclonal paraprotein 18g/l

Bone Marrow examination showing 6% plasma cells

Skeletal Survey showing no abnormalities

What is the diagnosis?

- ☐ Multiple Myeloma ×
- ☐ Hodgkins Lymphoma ×
- ☐ Waldenstrom's macroglobulinemia (lymphoplasmacytic lymphoma) ×

☐ Asymptomatic Myleoma ×

☐ Monoclonal gammopathy on uncertain significance (MGUS) ×

Submit answer

Reference ranges ▾

Score: **18%**

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An abnormal protein band is detected during analysis and the GP arranges for further review with the Haematologist at the hospital. Further investigations are undertaken:

- Monoclonal paraprotein 18g/l
- Bone Marrow examination showing 6% plasma cells
- Skeletal Survey showing no abnormalities

What is the diagnosis?

Multiple Myeloma	3%
Hodgkins Lymphoma	0%
Waldenstrom's macroglobulinemia (lymphoplasmacytic lymphoma)	12%

Monoclonal gammopathy on uncertain significance (MGUS)

82%

Monoclonal gammopathy on uncertain significance (MGUS) is a condition where an abnormal paraprotein is found in the blood, often during routine testing. It is on a spectrum that includes multiple myeloma but at the MGUS stage no treatment is indicated. The level of serum paraprotein is lower than in myeloma (under 30g/l) and the number of plasma cells in the bone marrow is also lower (less than 10%). The condition is totally asymptomatic. There is an annual risk of progression to myeloma of 1-2% and as such annual surveillance is recommended.

The diagnosis of MGUS can be made in patients who fulfil the following criteria -

- A monoclonal paraprotein band lesser than 30 g/L ($< 3\text{g/dL}$)
- Plasma cells less than 10% on bone marrow examination
- No evidence of bone lesions, anemia, hypercalcemia, or renal insufficiency related to the paraprotein
- No evidence of another B-cell proliferative disorder

In terms of myeloma this can be classified as below, taking note of both asymptomatic and symptomatic myeloma:

Symptomatic myeloma:

- Clonal plasma cells $>10\%$ on bone marrow biopsy or (in any quantity) in a biopsy from other tissues (plasmacytoma)
- A monoclonal protein (paraprotein) in either serum or urine (except in cases of true non-secretory myeloma)
- Evidence of end-organ damage felt related to the plasma cell disorder (related organ or tissue impairment, ROTI, commonly referred to by the acronym 'CRAB'):
- hyperCalcemia (corrected calcium $>2.75\text{mmol/L}$)
- Renal insufficiency attributable to myeloma
- Anemia (hemoglobin $<10\text{ g/dL}$)
- Bone lesions (lytic lesions or osteoporosis with compression fractures)

Asymptomatic (smoldering) myeloma:

- Serum paraprotein $>30\text{ g/L}$ AND/OR
- Clonal plasma cells $>10\%$ on bone marrow biopsy AND
- NO myeloma-related organ or tissue impairment



Discuss (5)

Improve

Next question >

Monoclonal gammopathy of undetermined significance (MGUS, also known as benign paraproteinaemia and monoclonal gammopathy) is a common condition that causes a paraproteinaemia and is often mistaken for myeloma. Differentiating features are listed below. Around 10% of patients eventually develop myeloma at 10 years, with 50% at 15 years

Features

- usually asymptomatic
- no bone pain or increased risk of infections
- around 10-30% of patients have a demyelinating neuropathy

Differentiating features from myeloma

- normal immune function
- normal beta-2 microglobulin levels
- lower level of paraproteinaemia than myeloma (e.g. < 30g/l IgG, or < 20g/l IgA)
- stable level of paraproteinaemia
- no clinical features of myeloma (e.g. lytic lesions on x-rays or renal disease)



123

[Next question >](#)**B***I***A****T**

Textbooks



[High-yield textbook](#)[Extended textbook](#)

Media



What is Monoclonal gammopathy of undetermined significance (MGUS)?

Khan Academy - YouTube

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[Report broken media](#)

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Question 66 of 89



You are the medical doctor on an acute admission unit. An elderly female with recently diagnosed ovarian cancer, who is on day 8 of cisplatin chemotherapy presents with a temperature of 39°C, tachycardia at 130 bpm, blood pressure 128/68 mmHg, respiratory rate 14/min, sats 98% on room air.

She is complaining of abdominal pain and has been vomiting today. Her bloods and blood culture have been sent and you are awaiting the results. Her chest x-ray was normal and urine dipstick clear.

What is the most appropriate antibiotic therapy to start her on?

- ☐ IV benzylpenicillin + flucloxacillin ×
- ☐ IV augmentin ×
- ☐ IV ciprofloxacin ×
- ☐ IV piperacillin/tazobactam ×
- ☐ IV piperacillin/tazobactam + gentamicin ×

Submit answer

Reference ranges 

Score: **18%**

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Question 66 of 89



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What is the most appropriate antibiotic therapy to start her on?

IV benzylpenicillin + flucloxacillin	1%
IV augmentin	0%
IV ciprofloxacin	1%
IV piperacillin/tazobactam	84%
IV piperacillin/tazobactam + gentamicin	13%

Piperacillin with tazobactam (Tazocin) is the empirical antibiotic of choice for neutropenic sepsis

Important for me Less important

The patient has presented with a systemic inflammatory response syndrome (SIRS) - tachycardia, pyrexia. The most likely cause for this would be an infection and she should be treated as a probable neutropenic sepsis until proven otherwise. Neutropenic sepsis tend to present on day 7-10 post-chemotherapy. Given that we are unable to determine the source of infection, she should ideally be treated with a broad-spectrum antibiotic such as IV piperacillin/tazobactam. You would also normally add a stat dose of gentamicin but given that she was on cisplatin therapy, the combination of these 2 medications would be highly nephrotoxic and should be withheld until neutropenic sepsis is confirmed and renal function results are available.



Discuss (9)

Improve

Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

NICE

👍 3 👎 1

[2012 Neutropenic sepsis guidelines](#)

Christies

👍 2 👎 4

[2013 Neutropenic sepsis guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Febrile Neutropenia](#)

Townsend Teaching - YouTube

👍 1 👎 0



[What is febrile neutropaenia \(neutropenia\)? - neutrophil function, pathophysiology, treatment](#)

Armando Hasudungan - YouTube

👍 2 👎 1



[Neutropenic sepsis](#)

Oncology for Medical Students - YouTube

👍 5 👎 3

Score: **20.2%**

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An 82-year-old man presents with a 6-month history of 8 kg of weight loss, fevers, and night sweats. On examination, he has cervical and inguinal lymphadenopathy and a mildly enlarged spleen. Blood results are as follows:

Hb	101 g/L	Male: (135-180) Female: (115 - 160)
Platelets	142 * 10 ⁹ /L	(150 - 400)
WBC	40.5 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	2.8 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	34 * 10 ⁹ /L	(1.0 - 3.5)

Given the most likely diagnosis, what would be the diagnostic investigation of choice?

- ☐ Bone marrow aspirate / trephine ×
- ☐ CT neck, chest, abdomen and pelvis ×
- ☐ Flow cytometry (immunophenotyping) ×
- ☐ HIV test ×
- ☐ Lymph node biopsy ×

Submit answer

Reference ranges 

Score: **18%**

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An 82-year-old man presents with a 6-month history of 8 kg of weight loss, fevers, and night sweats. On examination, he has cervical and inguinal lymphadenopathy and a mildly enlarged spleen. Blood results are as follows:

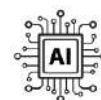
Hb	101 g/L	Male: (135-180) Female: (115 - 160)
Platelets	142 * 10 ⁹ /L	(150 - 400)
WBC	40.5 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	2.8 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	34 * 10 ⁹ /L	(1.0 - 3.5)

Given the most likely diagnosis, what would be the diagnostic investigation of choice?

Bone marrow aspirate / trephine	12%
CT neck, chest, abdomen and pelvis	2%
Flow cytometry (immunophenotyping)	65%
HIV test	0%
Lymph node biopsy	21%

CLL - immunophenotyping is investigation of choice

Important for me Less important



The diagnosis is most certainly CLL which is the most common cause of significant lymphocytosis in an elderly patient.

CLL has a very specific immunophenotype and can thus be diagnosed on **flow cytometry** of peripheral blood.

Although a **bone marrow examination** and **lymph node biopsy** would also likely be diagnostic of CLL, they are invasive tests and thus should only be performed if immunophenotyping was non-diagnostic.

A **CT neck, chest, abdomen, and pelvis** would be useful for staging, however, it would not be particularly helpful in making the diagnosis.

HIV can cause an early mild lymphocytosis (due to a CD8 lymphocytosis) however it is most often associated with lymphopaenia. The patient's age and presence of a marked lymphocytosis favour the diagnosis of CLL.



Discuss (6)

Improve

Next question >

Chronic lymphocytic leukaemia: features and investigation ★

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%). It is the most common form of leukaemia seen in adults.

Features

- often none: may be picked up by an incidental finding of lymphocytosis
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than chronic myeloid leukaemia

Investigations

- full blood count:
 - lymphocytosis
 - anaemia: may occur either due to bone marrow replacement or autoimmune hemolytic anaemia (AIHA)
 - thrombocytopenia: may occur either due to bone marrow replacement or immune thrombocytopenia (ITP)
- blood film: smudge cells (also known as smear cells)
- immunophenotyping is the key investigation
 - most cases can be identified using a panel of antibodies specific for CD5, CD19, CD20 and CD23

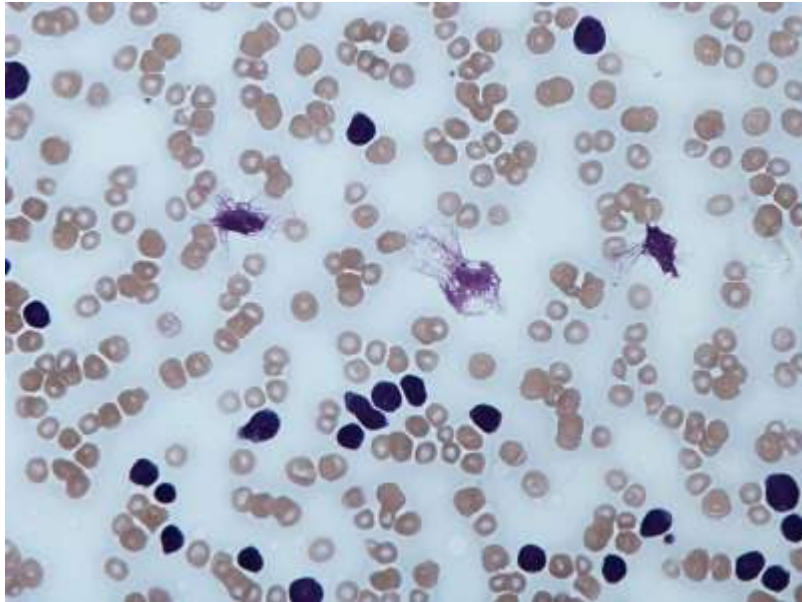


Image sourced from Wikipedia

Peripheral blood film showing smudge B cells



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123



Next question >

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A



T1



Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

👍 5 👎 4

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



Chronic Lymphocytic Leukemia (CLL) - Diagnosis & Treatment

Medicosis Perfectionalis - YouTube

👍 2 🗑 0



Chronic leukemia

Osmosis - YouTube

👍 2 🗑 0



Chronic Lymphocytic Leukemia (CLL)

Medicosis Perfectionalis - YouTube

👍 1 🗑 0



Chronic leukaemia

Khan Academy - YouTube

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Question 68 of 89



A 39-year-old woman presents with anaemia secondary to menorrhagia. She has a past medical history of fibroids, rhesus incompatibility in pregnancy 9 years ago, and Hodgkin's lymphoma which has been in remission for 21 years.

She has a severe penicillin allergy.

Her investigations show the following:

Hb	59 g/L	Female: (115 - 160)
Platelets	$350 \times 10^9/L$	(150 - 400)
WBC	$4.7 \times 10^9/L$	(4.0 - 11.0)

Pregnancy test: negative.

The consultant asks for you to prescribe her 2 units of packed red cells.

What requirement would apply to this patient's blood transfusion?

- ☐ Give antihistamines with packed red cells ×
- ☐ No special requirements ×
- ☐ Use CMV negative packed red cells ×
- ☐ Use irradiated packed red cells ×
- ☐ Use washed red blood cells ×

Submit answer

Reference ranges 

Score: **18%**

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Pregnancy test: negative.

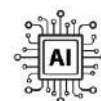
The consultant asks for you to prescribe her 2 units of packed red cells.

What requirement would apply to this patient's blood transfusion?

Give antihistamines with packed red cells	1%
No special requirements	14%
Use CMV negative packed red cells	10%
Use irradiated packed red cells	68%
Use washed red blood cells	6%

Hodgkin lymphoma is an indication for irradiated blood products

Important for me Less important




The patient would require **irradiated** packed red cells due to her history of Hodgkin's lymphoma. Irradiated blood is treated with radiation which prevents lymphocyte division which can cause transfusion-associated graft-versus-host disease (TA-GvHD). A history of Hodgkin's lymphoma increases the risk of this reaction and hence all red cell, platelet, and granulocyte concentrates should be irradiated for life.

No special requirements is incorrect because this patient requires irradiated blood as explained above.

There is no indication for **antihistamines** to be given with packed red cells for this patient. Like all patients, she should be monitored for any signs of allergic reaction regularly during her transfusion but only treated for this if this occurs.

CMV negative blood is blood collected from donors who have tested negative for CMV IgG antibodies. CMV can cause serious infections in immunocompromised patients and is the most common cause of congenital infection cause developmental abnormalities in the UK. CMV negative blood should be used for intrauterine transfusions, neonates up to 28 days post expected delivery and for transfusions during pregnancy. There is no indication for CMV negative blood in this patient.

Washed red cells are used when there are recurrent and/or severe allergic reactions to transfusion and can also be used for IgA deficient patients with anti-IgA antibodies. This patient has a penicillin allergy but not to blood products.

   Discuss (4)  Improve

Next question >

Blood products: CMV negative and irradiated blood ★

Cytomegalovirus (CMV) is transmitted in leucocytes. As most blood products (except granulocyte transfusions) are now leucocyte depleted CMV negative products are rarely required.

Irradiated blood products are depleted of T-lymphocytes and used to avoid transfusion-associated graft versus host disease (TA-GVHD) caused by engraftment of viable donor T lymphocytes.

The table below shows the indications for CMV and irradiated blood:

Situation	CMV negative	Irradiated
Granulocyte transfusions	✓	✓
Intra-uterine transfusions	✓	✓
Neonates up to 28 days post expected date of delivery	✓	✓
Pregnancy: Elective transfusions during pregnancy (not during labour or delivery)	✓	

Situation	CMV negative	Irradiated
Bone marrow / stem cell transplants		✓
Immunocompromised (e.g. chemotherapy or congenital)		✓
Patients with/previous Hodgkin lymphoma		✓
HIV		



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

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Question 69 of 89



A 47-year-old woman with a background of obesity is admitted with left leg cellulitis. Blood cultures are taken and she is commenced on IV flucloxacillin.

Shortly afterwards, you are asked to see her as she has become itchy and light-headed in the last 5 minutes. Observations are as follows.

- Respiratory rate 30 breaths per minute
- Oxygen saturations 90% on air
- Heart rate 127 beats per minute
- Blood pressure 75/42mmHg
- Temperature 36.8°C

Chest examination reveals widespread wheeze. The rest of the examination is unremarkable, other than her cellulitis which has not spread beyond the markings.

What statement is correct concerning the suspected diagnosis?

☐ An elevated tryptase that remains at the same level after 2 hours supports the diagnosis



☐ High tryptase now confirms the diagnosis



☐ Normal tryptase at 24 hours excludes the diagnosis



☐ Normal tryptase now excludes the diagnosis



☐ Normal tryptase now that becomes elevated in 2 hours supports the diagnosis



Submit answer

Reference ranges 

Score: **18%**

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Question 69 of 89



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- Temperature 36.8°C

Chest examination reveals widespread wheeze. The rest of the examination is unremarkable, other than her cellulitis which has not spread beyond the markings.

What statement is correct concerning the suspected diagnosis?

An elevated tryptase that remains at the same level after 2 hours supports the diagnosis 26%

High tryptase now confirms the diagnosis 21%

Normal tryptase at 24 hours excludes the diagnosis 5%

Normal tryptase now excludes the diagnosis 5%

Normal tryptase now that becomes elevated in 2 hours supports the diagnosis 43%

Anaphylaxis - serum tryptase levels rise following an acute episode

Important for me Less important

The correct answer is **normal tryptase now that becomes elevated in 2 hours supports the diagnosis**. The features of cardiovascular collapse, breathing difficulty and bronchospasm following IV antibiotics are suggestive of anaphylaxis. Tryptase is released into the blood in the context of mast cell degranulation. In anaphylaxis, it is expected to rise quickly in the first minutes to hours before gradually falling. NICE recommend it is measured at baseline and after 1-2 hours (but no later than 4). If measured at onset, it may be normal - the key finding is the elevation over the first few hours. If measured after 4 hours, it may have returned to normal.

An elevated tryptase that remains at the same level after 2 hours supports the diagnosis is incorrect. Some patients have elevated tryptase at baseline, for example in the context of systemic

mastocytosis. It can also cross-react, for example with rheumatoid factors, leading to elevated levels in the absence of anaphylaxis. The lack of a change over 2 hours is more suggestive of a high baseline rather than anaphylaxis, where we would expect a significant change from onset to 2 hours.

High tryptase now confirms the diagnosis is incorrect. A single elevated measurement does not confirm the diagnosis for the reasons described above - a second sample must be taken within the next few hours to check for a change from baseline.

Normal tryptase at 24 hours excludes the diagnosis is incorrect. By 24 hours, we would expect the tryptase level to have returned to baseline, even in a significant anaphylactic episode. A baseline level and a 1-2 hour level would be much more helpful.

Normal tryptase now excludes the diagnosis. Tryptase level at the onset of symptoms may be normal as it takes at least 15 minutes (but longer in some patients) to mount a response, and we are told the symptoms have lasted 5 minutes here. A single measurement has limited utility, and we would have to repeat the sample at 1-2 hours for more useful information.

		 Discuss (3)	Improve
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Next question >

Anaphylaxis ★

Anaphylaxis may be defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction.

Common identified causes of anaphylaxis:

- food (e.g. nuts) - the most common cause in children
- drugs
- venom (e.g. wasp sting)

Features

The Resus Council UK define anaphylaxis as:

- the sudden onset and rapid progression of symptoms
- **A**irway and/or **B**reathing and/or **C**irculation problems
- **A**irway problems may include:
 - swelling of the throat and tongue → hoarse voice and stridor
- **B**reathing problems may include:
 - respiratory wheeze
 - dyspnoea
- **C**irculation problems may include:

- hypotension
- tachycardia

This means that if there are no ABC problems then the patient is technically not having anaphylaxis.

Around 80-90% of patients also have skin and mucosal changes:

- generalised pruritus
- widespread erythematous or urticarial rash

Management

Anaphylaxis is one of the few times when you would not have time to look up the dose of a medication. The Resuscitation Council guidelines on anaphylaxis have recently been updated. **Intramuscular adrenaline** is by far the most important drug in anaphylaxis and should be given as soon as possible. Previously IV hydrocortisone was also recommended but the evidence base for this was poor and it was removed in the 2021 update.

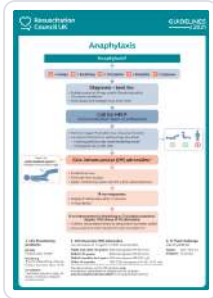
The recommended doses for adrenaline are as follows: **BNF**

Age	Adrenaline dose
< 6 months	100 - 150 micrograms (0.1 - 0.15 ml 1 in 1,000)
6 months - 6 years	150 micrograms (0.15 ml 1 in 1,000)
6-12 years	300 micrograms (0.3ml 1 in 1,000)
Adult and child > 12 years	500 micrograms (0.5ml 1 in 1,000)

Adrenaline can be repeated every 5 minutes if necessary. The best site for IM injection is the anterolateral aspect of the middle third of the thigh.

Refractory anaphylaxis

- defined as respiratory and/or cardiovascular problems persist despite 2 doses of IM adrenaline
- IV fluids should be given for shock
- expert help should be sought for consideration of an IV adrenaline infusion



Management following stabilisation:

- non-sedating oral antihistamines, in preference to chlorphenamine, may be given following initial stabilisation especially in patients with persisting skin symptoms (urticaria and/or angioedema)
- sometimes it can be difficult to establish whether a patient had a true episode of anaphylaxis. Serum **tryptase** levels are sometimes taken in such patients as they remain elevated for up to 12 hours following an acute episode of anaphylaxis
- all patients with a new diagnosis of anaphylaxis should be referred to a specialist allergy clinic
- an adrenaline injector should be given as an interim measure before the specialist allergy assessment (unless the reaction was drug-induced)
 - patients should be prescribed 2 adrenaline auto-injectors
 - training should be provided on how to use it
- a risk-stratified approach to discharge should be taken as biphasic reactions can occur in up to 20% of patients

The Resus Council UK recommend the following risk-stratified approach to discharge:

- fast-track discharge (after 2 hours of symptom resolution):
 - good response to a single dose of adrenaline
 - complete resolution of symptoms
 - has been given an adrenaline auto-injector and trained how to use it
 - adequate supervision following discharge
- minimum 6 hours after symptom resolution
 - 2 doses of IM adrenaline needed, or
 - previous biphasic reaction
- minimum 12 hours after symptom resolution
 - severe reaction requiring > 2 doses of IM adrenaline
 - patient has severe asthma
 - possibility of an ongoing reaction (e.g. slow-release medication)
 - patient presents late at night
 - patient in areas where access to emergency access care may be difficult
 - observation for at 12 hours following symptom resolution



123



Next question >



Textbooks

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Links

Clinical Knowledge Summaries

 1  0



[Angio-oedema and anaphylaxis](#)

Resus Council

 3  1

[Anaphylaxis guidelines](#)

BNF

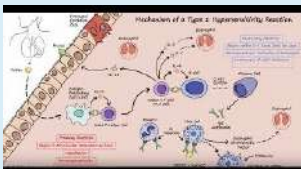
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[Medical emergencies in the community](#)



[Suggest link](#)

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Media



[Type I Hypersensitivity](#)

PhysioPathoPharmaco - YouTube  3  2



[Type I hypersensitivity](#)

Osmosis - YouTube

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Question 70 of 89



A 17-year-old man presents to the acute medical unit with shortness of breath. He takes no regular medicines and denies the use of any recreational, herbal, or over-the-counter medications. He has not been exposed to any local anaesthetics or chemicals. On examination, his chest was clear on auscultation and he was markedly cyanotic. Despite the cyanosis, his SpO₂ is 92%.

You start the patient on 15L O₂ via a non-rebreather mask.

Blood gas analysis results are as follows:

pH	7.28	(7.35 - 7.45)
PaO ₂	66.5 kPa	(10.3 - 13.3 kPa)
PaCO ₂	2.8 kPa	(4.7 - 6 kPa)
HCO ₃	22 mmol/L	(22 - 28 mmol/L)
SaO ₂	52%	(94-98)

The patient moved to the UK from India 6 weeks ago. His medical records are not available. However, he advises you that he has a 'blood disorder' that runs in his family.

Given the most likely diagnosis, what is the treatment of choice?

- ☐ 4-Dimethylaminophenol ×
- ☐ Ascorbic acid ×
- ☐ C1-inhibitor concentrate ×
- ☐ Hydroxocobalamin ×
- ☐ Hyperbaric oxygen ×

Submit answer

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A 17-year-old man presents to the acute medical unit with shortness of breath. He takes no regular medicines and denies the use of any recreational, herbal, or over-the-counter medications. He has not been exposed to any local anaesthetics or chemicals. On examination, his chest was clear on auscultation and he was markedly cyanotic. Despite the cyanosis, his SpO₂ is 92%.

You start the patient on 15L O₂ via a non-rebreather mask.

Blood gas analysis results are as follows:

pH	7.28	(7.35 - 7.45)
PaO ₂	66.5 kPa	(10.3 - 13.3 kPa)
PaCO ₂	2.8 kPa	(4.7 - 6 kPa)
HCO ₃	22 mmol/L	(22 - 28 mmol/L)
SaO ₂	52%	(94-98)

The patient moved to the UK from India 6 weeks ago. His medical records are not available. However, he advises you that he has a 'blood disorder' that runs in his family.

Given the most likely diagnosis, what is the treatment of choice?

4-Dimethylaminophenol	9%
Ascorbic acid	68%
C1-inhibitor concentrate	4%
Hydroxocobalamin	12%
Hyperbaric oxygen	8%

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency

Important for me Less important

The striking feature, in this case, is the significant discrepancy between the PaO₂ and SaO₂. Given the patient is on 15L O₂, the PaO₂ is at a level expected indicating that gas exchange at the level of the alveoli is not impaired. However, the SaO₂ is markedly low at 52% indicating impaired oxygen binding to haemoglobin. The main two causes of this picture are methaemoglobinaemia


and carboxyhemoglobinemia. The family history is indicative of familial NADH methaemoglobinaemia reductase deficiency.

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency.

Hyperbaric oxygen is the treatment of choice for severe carbon monoxide poisoning. Although carbon monoxide poisoning presents similarly and remains within the differential diagnosis, the positive family history makes congenital methaemoglobinaemia the more likely diagnosis.

4-Dimethylaminophenol and **hydroxocobalamin** can be used for the treatment of cyanide poisoning. Cyanide binds the ferric (Fe^{3+}) ion of cytochrome oxidase causing 'histotoxic hypoxia' and lactic acidosis. It would not cause a marked reduction of SaO_2 as seen in this case unless it was associated with coexistent carbon monoxide poisoning (e.g. due to smoke inhalation). There is nothing in this case to suggest that this is the case.

C1-inhibitor concentrate remains the gold standard treatment for the acute management of hereditary angioedema. The clinical and laboratory features, in this case, are not in keeping with hereditary angioedema which presents with recurrent attacks of self-limiting oedema affecting the skin, gastrointestinal tract, and airways.

		 Discuss (4)	Improve
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Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO₂ but decreased oxygen saturation

Management

- NADH methaemoglobinemia reductase deficiency: ascorbic acid
- IV methylnthioninium chloride (methylene blue) if acquired



123



Next question >

B

I



A



T



Textbooks

High-yield textbook

Extended textbook

Links

Life in the Fast Lane



6



3

[Methaemoglobinemia](#)

The Internet Book of Critical Care



10



4

[Methemoglobinemia](#)



[Suggest link](#)

[Report broken link](#)

Media



Methaemoglobinaemia

Osmosis - YouTube  7  2

[Report broken media](#)

Score: **20.2%**

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Question 71 of 89



A 36-year-old man is brought to the emergency department following a motor vehicle accident. He is drowsy but conscious. He has an open fracture on the right anterior shin which is bleeding profusely. Vital sign monitoring reveals that he has a respiratory rate of 22 bpm, heart rate of 118 bpm, blood pressure of 92/55 mmHg and temperature of 37.1 degrees Celsius. In an attempt to resuscitate the patient, the doctor decides to transfuse 2 pints of group O negative blood. A few minutes after giving the blood, the nurse notices that the patient developed a generalized rash and swelling of the lips, associated with a loud breathing sound. His medical notes reveal that he has atopy and has been treated for giardiasis multiple times previously. Which one of the following conditions could possibly represent a predisposition to the patient's condition?

- ☐ Von Willebrand disease ×
- ☐ Hairy cell leukemia ×
- ☐ Selective IgA deficiency ×
- ☐ Severe combined immunodeficiency ×
- ☐ Wiskott-Aldrich syndrome ×

Submit answer

Reference ranges 

Score: **18%**

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Von Willebrand disease	1%
Hairy cell leukemia	1%
Selective IgA deficiency	77%
Severe combined immunodeficiency	10%
Wiskott-Aldrich syndrome	11%

IgA deficiency is associated with anaphylactic reaction to blood products

Important for me Less important

This patient presented after a motor vehicle accident with an open fracture wound. The vital signs pointed towards a hypovolemic shock secondary to blood loss from the fracture wound and also possibly secondary to an internal injury, such as a spleen laceration. The patient was transfused with group O negative blood, which is the universal donor blood group, but developed an anaphylactic reaction. This is quite unusual given that the blood was group O negative. Anaphylactic reactions to products are common among individuals with selective IgA deficiency. Selective IgA deficiency is the most common primary immunodeficiency and individuals with this condition have low IgA levels despite normal levels of the IgG and IgM. Patients often suffer from recurrent airway infections, atopy, autoimmune diseases and are prone to have giardiasis infection. To avoid this, these patients must receive blood products without IgA. (First Aid 2017, p110 & p112)

- 1: Von Willebrand disease is a coagulation disorder which affects intrinsic pathway and is due to deficient von Willebrand factor. This leads to an impairment in the formation of the platelet plug. There is no increased risk of anaphylaxis to blood products in patients with this condition.
- 2: Hairy cell leukemia is one type of lymphoid neoplasm with the cells having hair-like projections

and hence the name of the condition. The disease leads to bone marrow fibrosis. There is no increased risk of anaphylaxis to blood products in patients with this condition.

4: Severe combined immunodeficiency is a type of immunodeficiency which involves both a B and T-cell disorder. There are different types comprising IL-2R gamma chain deficiency and adenosine deaminase deficiency. Patients often present with failure to thrive, thrush and diarrhea. They have an increased susceptibility to infections from several types of microorganisms such as viruses, fungi, protozoan, and bacteria. There is no increased risk of anaphylaxis to blood products in patients with this condition.

5: Wiskott-Aldrich syndrome is a type of immunodeficiency which involves both a B and T-cell disorder. It is due to a mutation on the WASp gene causing platelets and leukocytes to be unable to carry out antigen presentation due to a defective actin cytoskeletal reorganization. Patients often present with the triad of thrombocytopenia, recurrent pyogenic infections, and eczema. There is no increased risk of anaphylaxis to blood products in patients with this condition.



Discuss (1)

Improve

Next question >

Primary immunodeficiency ★

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
Chronic granulomatous disease	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. <i>Staphylococcus aureus</i> and fungi (e.g. <i>Aspergillus</i>) Negative nitroblue-tetrazolium test Abnormal dihydrorhodamine flow cytometry test
Chediak-Higashi syndrome	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen Giant granules in neutrophils and platelets

Disorder	Underlying defect	Notes
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen Absence of neutrophils/pus at sites of infection

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Low antibody levels, specifically in immunoglobulin (Ig) types IgG, IgM and IgA. Recurrent chest infections. May also predispose to autoimmune disorders and lymphoma
Bruton's (x-linked) congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen Absence of B-cells with reduced immunoglobulins of all classes
Selective immunoglobulin A deficiency	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and respiratory infections Associated with coeliac disease and may cause false negative coeliac antibody screen Severe reactions to blood transfusions may occur (anti-IgA antibodies → anaphylaxis)

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4th pharyngeal pouches	Common features include congenital heart disease (e.g. tetralogy of Fallot), learning difficulties, hypocalcaemia, recurrent viral/fungal diseases, cleft palate

Combined B- and T-cell disorders

Disorder	Underlying defect	Notes
Severe combined immunodeficiency	Many varying causes. Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. Other causes include adenosine deaminase deficiency	Recurrent infections due to viruses, bacteria and fungi. Reduced T-cell receptor excision circles Stem cell transplantation may be successful
Ataxic telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia (spider angiomas), recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopenia. Low IgM levels Increased risk of autoimmune disorders and malignancy
Hyper IgM Syndromes	Mutations in the CD40 gene	Infection/ <i>Pneumocystis</i> pneumonia, hepatitis, diarrhoea



123



Next question >

B

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Textbooks

High-yield textbook

Extended textbook

Media



[X linked agammaglobulinemia \(Bruton agammaglobulinemia\)](#)

Osmosis - YouTube

👍 1 👎 0



[Well defined genetic immunodeficiency - DiGeorge Syndrome and Job Syndrome](#)

Armando Hasudungan - YouTube

👍 4 👎 1



[Leukocyte adhesion deficiency](#)

Osmosis - YouTube

👍 4 👎 1



[Selective immunoglobulin A deficiency](#)

Osmosis - YouTube

👍 2 👎 1



Primary antibody deficiency - Common Variable Immunodeficiency (CVID) , X-linked agammaglobulinemia

Armando Hasudungan - YouTube

👍 2 👎 2



Digeorge syndrome (22q11.2 deletion syndrome)

Osmosis - YouTube

👍 0 👎 1

[Report broken media](#)

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Question 72 of 89



A 35-year-old patient presents to a rural emergency department with abdominal pain and facial swelling. He has a past medical history of C1 esterase inhibitor deficiency. He has recently arrived from Belarus and does not have any of his regular medications. He does not smoke cigarettes or drink alcohol.

His observations are heart rate 88 beats per minute, blood pressure 122/78mmHg, respiratory rate 18/minute, oxygen saturations 96% on room air and temperature 37°C.

On examination, there is facial swelling without airway compromise. There is mild abdominal tenderness without any evidence of peritonism. There is no rash or wheeze.

Unfortunately, there is no possibility of locating IV C1-inhibitor concentrate in this rural setting.

Given the clinical history, what is the most appropriate medication to abort the attack?

- | | | |
|-----------------------|---------------------|---|
| <input type="radio"/> | Adrenaline | × |
| <input type="radio"/> | Danazol | × |
| <input type="radio"/> | Fexofenadine | × |
| <input type="radio"/> | Fresh frozen plasma | × |
| <input type="radio"/> | Prednisolone | × |

Submit answer

Reference ranges 

Score: **18%**

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On examination, there is facial swelling without airway compromise. There is mild abdominal tenderness without any evidence of peritonism. There is no rash or wheeze.

Unfortunately, there is no possibility of locating IV C1-inhibitor concentrate in this rural setting.

Given the clinical history, what is the most appropriate medication to abort the attack?

Adrenaline	5%
Danazol	19%
Fexofenadine	4%
Fresh frozen plasma	67%
Prednisolone	6%

Hereditary angioedema: the acute management is IV C1-inhibitor concentrate or fresh frozen plasma if this is not available

Important for me Less important

Fresh frozen plasma is the correct answer. This is an available option for treating acute attacks of hereditary angioedema (HAE) if IV C1-inhibitor concentrate is not available.

Danazol is incorrect. This is a gonadotropin inhibitor used in the prophylaxis of HAE rather than in the management of acute attacks.

Fexofenadine, prednisolone and adrenaline are all incorrect. They are ineffective in managing the swelling associated with this condition. The postulated theory is that histamine-mediated angioedema responds to these interventions but bradykinin mediated angioedema is resistant. Bradykinin is the principal mediator of symptoms in HAE.

Hereditary angioedema ★

Hereditary angioedema (HAE) is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH, C1 esterase inhibitor) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

Symptoms

- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

Management

- acute
 - HAE does not respond to adrenaline, antihistamines, or glucocorticoids
 - IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help



Textbooks

High-yield textbook

Extended textbook

Links

Patient.info

 1  4

[Hereditary angioedema review](#)

[Suggest link](#)



[Report broken link](#)

Media



[The Role of the C1-Esterase Inhibitor in HAE](#)

Individual - YouTube

 3  0

[Report broken media](#)

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A 73-year-old woman is reviewed routinely in haematology clinic. She has a diagnosis of chronic lymphocytic leukaemia. She is not on any treatment but remains under regular review. She has lost 5% of her body weight in the last 9 months. She reports occasional fatigue. She does not smoke cigarettes or drink alcohol. She lives alone and is independent.

On examination, there are two 0.5cm lymph nodes palpable in her neck, which were palpable at her previous appointment.

Blood tests at the time of clinic review:

Hb	122 g/L	Male: (135-180) Female: (115 - 160)
Platelets	75 * 10 ⁹ /L	(150 - 400)
WBC	14 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	6.0 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	7.8 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.0 * 10 ⁹ /L	(0.0 - 0.4)

Blood tests two months ago:

Hb	123 g/L	Male: (135-180) Female: (115 - 160)
Platelets	189 * 10 ⁹ /L	(150 - 400)
WBC	13.5 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	6 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	7.3 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.0 * 10 ⁹ /L	(0.0 - 0.4)

What patient-specific factor does this patient possess that warrants commencing treatment for her underlying malignancy?

☐ Fatigue

☐ Weight loss


<input type="radio"/>	Lymphadenopathy	×
<input type="radio"/>	Progressive lymphocytosis	×
<input type="radio"/>	Thrombocytopenia	×

Submit answer

Reference ranges ▾

Score: 18%		
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9	✓	
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A 73-year-old woman is reviewed routinely in haematology clinic. She has a diagnosis of chronic lymphocytic leukaemia. She is not on any treatment but remains under regular review. She has lost 5% of her body weight in the last 9 months. She reports occasional fatigue. She does not smoke cigarettes or drink alcohol. She lives alone and is independent.

On examination, there are two 0.5cm lymph nodes palpable in her neck, which were palpable at her previous appointment.

Blood tests at the time of clinic review:

Hb	122 g/L	Male: (135-180) Female: (115 - 160)
Platelets	75 * 10 ⁹ /L	(150 - 400)
WBC	14 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	6.0 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	7.8 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.0 * 10 ⁹ /L	(0.0 - 0.4)

Blood tests two months ago:

Hb	123 g/L	Male: (135-180) Female: (115 - 160)
Platelets	189 * 10 ⁹ /L	(150 - 400)
WBC	13.5 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	6 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	7.3 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.0 * 10 ⁹ /L	(0.0 - 0.4)

What patient-specific factor does this patient possess that warrants commencing treatment for her underlying malignancy?

Fatigue

3%

Weight loss

17%

Lymphadenopathy

3%

Progressive lymphocytosis

6%

Thrombocytopenia

72%

Thrombocytopenia -> indication to start treatment in CLL

Important for me Less important

Thrombocytopenia is the correct answer. The development of thrombocytopenia is an indication to start treatment in CLL.

Fatigue is incorrect. While extreme fatigue may be an indication to start treatment, this patient reports only occasional fatigue and therefore treatment is not warranted on this basis.

Progressive lymphocytosis is incorrect. This patient has a < 50% increase in lymphocyte count over the course of two months and therefore does not meet criteria to start treatment on this basis.

Lymphadenopathy is incorrect. The lymphadenopathy needs to be either massive (>10cm) or progressive to warrant treatment and it is neither.

Weight loss is incorrect. This patient has lost 5% of her body weight in 9 months. She would need to have lost 10% in approximately six months to warrant treatment.



Discuss (2)

Improve

Next question >

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (> 10 cm) or progressive lymphadenopathy
- massive (> 6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever > 38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy



123



Next question >

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Textbooks

High-yield textbook

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Links

British Committee for Standards in Haematology



3



4

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)

Medicosis Perfectionalis - YouTube



3



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Chronic leukemia

Osmosis - YouTube

2 2

[Report broken media](#)

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A 67-year-old male with known chronic lymphocytic leukaemia (CLL) currently under monitoring only presents to his general practitioner. He has developed new fevers and reports his pillow being wet. He has a dry cough and has lost a few pounds in weight but otherwise feels well. He is otherwise well and has hypertension and type 2 diabetes. He was taking amlodipine, metformin and tolbutamide but has stopped these two weeks prior due to his prescription not being renewed. He is a smoker and drinks alcohol 10-14 units a week.

On examination, his temperature is 37.9°C and his chest is clear. He is clammy but there are no visible rashes.

Hb	124 g/l
Platelets	378 * 10 ⁹ /l
WBC	13.2 * 10 ⁹ /l
Neuts	11.2* 10 ⁹ /l
CRP	9mg/L
LDH	857 U/L (normal range 180-360 U/L)

What is the likely explanation?

- ☐ Drug withdrawal reaction ×
- ☐ Richter's transformation ×
- ☐ Lower respiratory tract infection (LRTI) ×
- ☐ Glandular fever ×
- ☐ Neutropaenic sepsis ×

Submit answer

Reference ranges 

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On examination, his temperature is 37.9°C and his chest is clear. He is clammy but there are no visible rashes.

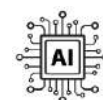
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WBC	13.2 * 10 ⁹ /l
Neuts	11.2* 10 ⁹ /l
CRP	9mg/L
LDH	857 U/L (normal range 180-360 U/L)

What is the likely explanation?

Drug withdrawal reaction	7%
Richter's transformation	82%
Lower respiratory tract infection (LRTI)	4%
Glandular fever	6%
Neutropaenic sepsis	2%

New B-symptoms in CLL -> Richter's transformation

Important for me Less important



This gentleman presents with new fevers and night sweats on a background of CLL which is normally controlled. He notably has a raised lactate dehydrogenase (LDH) and these symptoms in the context of haematology are B-symptoms. He is not neutropenic. Glandular fever would not

explain the night sweats and fevers and usually presents with fatigue and a sore throat. The medications would not cause isolated fever as a withdrawal reaction. A LRTI is possible but there is only a dry cough and no chest signs. We know that 5% of CLL will undergo Richter's transformation becoming a high grade lymphoma with new B-symptoms and crucially a rise in LDH which makes this the likeliest answer.

Discuss (4)

Improve

[Next question >](#)

Chronic lymphocytic leukaemia: complications ★

Complications

- anaemia
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Richter's transformation

Richter's transformation occurs when leukaemia cells enter the lymph node and change into a high-grade, fast-growing non-Hodgkin's lymphoma. Patients often become unwell very suddenly.

Richter's transformation is indicated by one of the following symptoms:

- lymph node swelling
- fever without infection
- weight loss
- night sweats
- nausea
- abdominal pain

[Next question >](#)

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Textbooks

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Media



Chronic Lymphocytic Leukemia (CLL)

Medicosis Perfectionalis - YouTube

👍 4 🗨 0



Chronic Lymphocytic Leukemia (CLL) - Diagnosis & Treatment

Medicosis Perfectionalis - YouTube

👍 2 🗨 0

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Score: **20.2%**

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Question 75 of 89



A 53-year-old man presents with abdominal pain. He was seen six weeks ago by surgeons who diagnosed gastritis and offered omeprazole. He initially improved but the pain recurred and he has no benefit with omeprazole or gaviscon. He feels full quickly but has no dysphagia or regurgitation. He denies any heartburn. He reports general low energy and is sleeping more hours in the day and can fall asleep at any time.

On examination, a mass is palpable in the epigastrium. It has a palpable indent and you cannot get above it. There are bowel sounds and no other masses are felt. There are some isolated left axillary lymph nodes palpable. His temperature is 37.8°C and heart rate is 78 beats per minute.

Hb	114 g/l
Platelets	289 * 10 ⁹ /l
WBC	51 * 10 ⁹ /l

What is the likeliest underlying diagnosis?

- ☐ Gastric carcinoma ×
- ☐ Visceral leishmaniasis ×
- ☐ Chronic myelogenous leukaemia (CML) ×
- ☐ Obstructive sleep apnoea (OSA) ×
- ☐ Narcolepsy ×

Submit answer

Reference ranges 

Score: **18%**

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Hb	114 g/l
Platelets	289 * 10 ⁹ /l
WBC	51 * 10 ⁹ /l

What is the likeliest underlying diagnosis?

Gastric carcinoma	18%
Visceral leishmaniasis	4%
Chronic myelogenous leukaemia (CML)	77%
Obstructive sleep apnoea (OSA)	1%
Narcolepsy	0%

CML may present with massive splenomegaly

Important for me [Less important](#)

This gentleman presents with abdominal pain and a new mass that based on location is likely spleen, stomach or left kidney. OSA and narcolepsy explain the sleepiness but not the abdominal symptoms. Gastric carcinoma with outlet obstruction can give a mass but usually there is vomiting or regurgitation of food contents. The mass is therefore likely to be spleen of which CML and leishmaniasis are the commonest causes. Leishmaniasis is less common making CML the likeliest diagnosis. Furthermore, the WBC is through the roof supporting CML as the cause.

Chronic myeloid leukaemia ★

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein that has tyrosine kinase activity in excess of normal.

Presentation (60-70 years)

- anaemia: lethargy
- weight loss and sweating are common
- splenomegaly may be marked → abdo discomfort
- an increase in granulocytes at different stages of maturation +/- thrombocytosis
- decreased leukocyte alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management

- imatinib is now considered first-line treatment
 - inhibitor of the tyrosine kinase associated with the BCR-ABL defect
 - very high response rate in chronic phase CML
- hydroxyurea
- interferon-alpha
- allogenic bone marrow transplant



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Textbooks

High-yield textbook

Links

Clinical Knowledge Summaries

👍 12 🗑️ 10

[Haematological cancers - recognition and referral](#)

[Suggest link](#)

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Media



[Chronic myeloid leukaemia](#)

Khan Academy - YouTube 👍 0 🗑️ 0



[Chronic leukemia](#)

Osmosis - YouTube 👍 0 🗑️ 0

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Score: **20.2%**

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A 12-year-old boy is referred by his paediatrician to a tertiary immunology service. Since infancy, he has suffered from recurrent infections. He has required multiple courses of antibiotics for episodes of sinusitis, otitis media and pneumonia. Heel prick testing was normal perinatally. The referral was ultimately made after he had a prolonged admission to the paediatric intensive care unit with respiratory failure requiring intubation, where he was diagnosed with *Pneumocystis jirovecii* pneumonia. HIV testing was negative. In addition to recurrent infections, he has had chronic diarrhoea, for which no cause has been found. He is on no regular medications. He does not smoke or drink alcohol and is doing well in school despite his frequent illnesses. His parents attend the appointment with him.

Clinical examination revealed a thin adolescent. There was evidence of stomatitis and gingivitis. There was no organomegaly or lymphadenopathy. The cardiovascular and respiratory examination was unremarkable. There were no rashes. Neurological examination is unremarkable.

Blood tests:

Hb	124 g/L	Male: (135-180) Female: (115 - 160)
Platelets	144 * 10 ⁹ /L	(150 - 400)
WBC	3.2 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	1.5 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	0.8 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.6 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.3 * 10 ⁹ /L	(0.0 - 0.4)
Na ⁺	136 mmol/L	(135 - 145)
K ⁺	4.4 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	77 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	8 µmol/L	(3 - 17)
ALP	77 u/L	(30 - 100)
ALT	16 u/L	(3 - 40)
Î ³ GT	44 u/L	(8 - 60)
Albumin	32 g/L	(35 - 50)
Immunoglobulin A	0.4 g/L	(0.6-5.0)

Immunoglobulin M	2.6 g/L	(0.53 - 2.47)
Immunoglobulin G	5.4 g/L	(6.60 - 15.90)

What is the likely diagnosis?

- ☐ Coeliac disease ×
- ☐ Cystic fibrosis ×
- ☐ Hyper IgM syndrome ×
- ☐ Malnutrition ×
- ☐ X-linked congenital agammaglobulinaemia ×

Submit answer

Reference ranges ∨

Score: **18%**

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Immunoglobulin M	2.6 g/L	(0.53 - 2.47)
Immunoglobulin G	5.4 g/L	(6.60 - 15.90)

What is the likely diagnosis?

Coeliac disease	6%
Cystic fibrosis	6%
Hyper IgM syndrome	63%
Malnutrition	1%
X-linked congenital agammaglobulinaemia	24%

Hyper IgM syndrome characteristically presents with infections e.g. *Pneumocystis pneumonia*, hepatitis, diarrhoea

Important for me [Less important](#)

Hyper IgM syndrome is correct. This is usually x-linked and therefore affects males. It is characterized by recurrent bacterial infections, chronic diarrhoea and infection with atypical organisms such as *Pneumocystis*. It may also be associated with autoimmune anaemia, neutropenia and thrombocytopenia. Patients often have stomatitis and gingivitis. IgM may either be normal or high. IgG and IgA will be low as the condition causes an inability to class switch from IgM.

Bruton's (x-linked) congenital agammaglobulinaemia is incorrect. This causes recurrent bacterial infections but all immunoglobulin subclasses will be low including IgM.

Cystic fibrosis is incorrect. While it would cause recurrent chest infections, heel prick testing as a newborn being normal makes this diagnosis unlikely.

Coeliac disease is incorrect. This can cause a thin habitus and diarrhoea but would not explain the other findings.

Malnutrition is incorrect. While this can predispose to infection, there is no reason to believe he is not being cared for properly. We are told he is doing well in school and has supportive parents that attend his hospital appointments.

Discuss (3)

Improve

[Next question >](#)

Primary immunodeficiency ★

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
Chronic granulomatous disease	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. <i>Staphylococcus aureus</i>) and fungi (e.g. <i>Aspergillus</i>) Negative nitroblue-tetrazolium test Abnormal dihydrorhodamine flow cytometry test
Chediak-Higashi syndrome	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen Giant granules in neutrophils and platelets
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen Absence of neutrophils/pus at sites of infection

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Low antibody levels, specifically in immunoglobulin (Ig) types IgG, IgM and IgA. Recurrent chest infections. May also predispose to autoimmune disorders and lymphoma

Disorder	Underlying defect	Notes
Bruton's (x-linked) congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen Absence of B-cells with reduced immunoglobulins of all classes
<u>Selective immunoglobulin A deficiency</u>	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and respiratory infections Associated with coeliac disease and may cause false negative coeliac antibody screen Severe reactions to blood transfusions may occur (anti-IgA antibodies → anaphylaxis)

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4th pharyngeal pouches	Common features include congenital heart disease (e.g. tetralogy of Fallot), learning difficulties, hypocalcaemia, recurrent viral/fungal diseases, cleft palate

Combined B- and T-cell disorders

Disorder	Underlying defect	Notes
<u>Severe combined immunodeficiency</u>	Many varying causes. Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. Other causes include adenosine deaminase deficiency	Recurrent infections due to viruses, bacteria and fungi. Reduced T-cell receptor excision circles Stem cell transplantation may be successful

Disorder	Underlying defect	Notes
Ataxic telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia (spider angiomas), recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopaenia. Low IgM levels Increased risk of autoimmune disorders and malignancy
Hyper IgM Syndromes	Mutations in the CD40 gene	Infection/ <i>Pneumocystis</i> pneumonia, hepatitis, diarrhoea

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Next question >

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Textbooks

High-yield textbook

Extended textbook

Media



X linked agammaglobulinemia (Bruton agammaglobulinemia)

Osmosis - YouTube

👍 1 👎 0



Well defined genetic immunodeficiency - DiGeorge Syndrome and Job Syndrome

Armando Hasudungan - YouTube

👍 4 👎 1



Leukocyte adhesion deficiency

Osmosis - YouTube

👍 4 👎 1



Selective immunoglobulin A deficiency

Osmosis - YouTube

👍 2 👎 1



Primary antibody deficiency - Common Variable Immunodeficiency (CVID) , X-linked agammaglobulinemia

Armando Hasudungan - YouTube

👍 2 👎 2



Digeorge syndrome (22q11.2 deletion syndrome)

Osmosis - YouTube

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[Report broken media](#)

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A 74-year-old man is seen in the haematology clinic. He was diagnosed with chronic lymphocytic leukaemia 6 months ago following an incidental finding of lymphocytosis on some routine blood tests with his General Practitioner. He is currently under surveillance monitoring.

Over the last 6 months he has generally been in good health. He has occasional fatigue particularly towards the end of the day but remains to have a good appetite and reports no change in his weight. Only for the last week has he reported to be feeling more unwell with intermittent fevers and chills.

On examination he is febrile at 38.3°C. He is mildly tachycardic with a heart rate of 114bpm and a blood pressure of 133/79mmHg. His chest is clear and heart sounds are normal. His abdomen is soft and non-tender. There is palpable 2cm splenomegaly.

Full blood count (6 months ago):

Hb	148 g/L	Male: (135-180) Female: (115 - 160)
WBC	49.3 * 10 ⁹ /L	(4.0 - 11.0)
Lymphocytes	46.3 * 10	(0.8 - 5.0)
Neutrophils	2.7 * 10	(2.5 - 7.5)
Platelets	200 * 10 ⁹ /L	(150 - 400)

Full blood count (today):

Hb	127 g/L	Male: (135-180) Female: (115 - 160)
WBC	75.6 * 10 ⁹ /L	(4.0 - 11.0)
Lymphocytes	69.4 * 10	(0.8 - 5.0)
Neutrophils	3.8 * 10	(2.5 - 7.5)
Platelets	102 * 10 ⁹ /L	(150 - 400)

Blood film: smudge cells seen.

Which of the following is an indication to start treatment in this patient?

- ☐ Splenomegaly ×
- ☐ Presence of fever for 1 week ×

- | | |
|---|---|
| <input type="radio"/> White cell count > 75 | × |
| <input type="radio"/> Presence of smudge cells on peripheral blood film | × |
| <input type="radio"/> Thrombocytopenia | × |

Submit answer

Reference ranges ▾

Score: **18%**

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Neutrophils	3.8 * 10	(2.5 - 7.5)
Platelets	102 * 10 ⁹ /L	(150 - 400)

Blood film: smudge cells seen.

Which of the following is an indication to start treatment in this patient?

- Splenomegaly

9%
- Presence of fever for 1 week

14%

White cell count > 75

16%

Presence of smudge cells on peripheral blood film

5%

Thrombocytopenia

56%

Thrombocytopenia -> indication to start treatment in CLL

Important for me Less important

This patient has a new thrombocytopenia compared to his blood tests 6 months ago. A new thrombocytopenia or sign of bone marrow failure is an indication to initiate treatment. Treatment options vary depending on the patient's overall health, co-morbidities and prognostic factors.

Massive splenomegaly > 5cm is an indicator to start treatment. However, this patient has a 2cm splenomegaly which does not make it an indicator for starting treatment.

Recurrent infections or fevers persisting beyond 2 weeks are indicators for starting treatment. This patient has had fevers for 1 week. However, if this continued then that would be a second indicator for starting treatment.

A rising lymphocyte count is an indicator for starting treatment. However, a doubling of lymphocytes in 6 months is needed which is not seen here.

Smudge cells are not an indicator for starting treatment.

Other indicators for starting treatment include: massive lymphadenopathy, constitutional symptoms including fever, weight loss or night sweats and the presence of haemolysis.



Discuss (2)

Improve

Next question >

Chronic lymphocytic leukaemia: management ★

Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (> 10 cm) or progressive lymphadenopathy
- massive (> 6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months

- systemic symptoms: weight loss > 10% in previous 6 months, fever >38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients
- ibrutinib may be used in patients who have failed a previous therapy



123



Next question >

B

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A



Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology



3



4

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)

Medicosis Perfectionalis - YouTube



3





2



Chronic leukemia

Osmosis - YouTube

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[Report broken media](#)

Score: **20.2%**

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A 45-year-old man is referred to the haematology clinic with a 4-month history of easy bruising and prolonged bleeding. He denies any other symptoms and is otherwise feeling well. His past medical history includes rheumatoid arthritis that he reports is not well-controlled, with frequent flares. There is no family history of bleeding disorders.

Laboratory blood tests:

Hb	126 g/L	(135-180)
Platelets	$201 \times 10^9/L$	(150 - 400)
WBC	$5.5 \times 10^9/L$	(4.0 - 11.0)
Prothrombin time (PT)	12 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	45 secs	(25-35 secs)
Fibrinogen	2.2 g/L	(2 - 4)
D-Dimer	300 ng/mL	(< 400)
Von Willebrand Factor	100 IU/dL	(50-150)
Factor VIII levels	Reduced	

What is the most likely diagnosis?

- ☐ Acquired haemophilia A ×
- ☐ Beta thalassaemia trait ×
- ☐ Christmas disease ×
- ☐ Factor V Leiden ×
- ☐ Von Willebrand's disease ×

Submit answer

Reference ranges 

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Laboratory blood tests:

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WBC	5.5 * 10 ⁹ /L	(4.0 - 11.0)
Prothrombin time (PT)	12 secs	(10-14 secs)
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Fibrinogen	2.2 g/L	(2 - 4)
D-Dimer	300 ng/mL	(< 400)
Von Willebrand Factor	100 IU/dL	(50-150)
Factor VIII levels	Reduced	

What is the most likely diagnosis?

Acquired haemophilia A	73%
Beta thalassaemia trait	1%
Christmas disease	6%
Factor V Leiden	3%
Von Willebrand's disease	17%

Acquired haemophilia A is diagnosed in patients without previous or familial histories of bleeding who have isolated prolongation of the activated partial thromboplastin time (aPTT), reduced FVIII levels as well as evidence of FVIII inhibitor activity

Important for me Less important

This patient has a diagnosis of acquired haemophilia A, an autoimmune disorder secondary to antibody production against factor VIII. Unlike congenital haemophilia A, acquired haemophilia A

develops later in life. Up to 50% of cases of acquired haemophilia A are associated with co-existing autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus and inflammatory bowel disease. The investigation findings are similar to congenital haemophilia A and include a raised aPTT and reduced FVIII levels. The presence of antibodies to factor VIII helps to differentiate between congenital and acquired causes.

Beta thalassaemia trait is a disorder of haemoglobin chain production, causing microcytic anaemia. Symptoms include those associated with anaemia such as pallor, shortness of breath and fatigue. Bruising and bleeding are not common features and beta thalassaemia trait does not explain this patient's clotting abnormalities.

Christmas disease (also known as haemophilia B) is an inherited coagulation disorder associated with reduced levels of factor IX. It has no impact on factor VIII levels and cannot explain this patient's laboratory findings.

Factor V Leiden (also known as activated protein C resistance) is the most common cause of thrombophilia. Rather than increasing bleeding, increased coagulation is seen, including an increased risk of deep vein thromboses. Therefore, factor V Leiden is incorrect.

Von Willebrand's disease is the most common inherited bleeding disorder. Symptoms include epistaxis, menorrhagia and gum bleeding. Similarly to this patient, coagulation studies demonstrate a prolonged APTT and reduced factor VIII levels. However, the presence of factor VIII inhibitor activity makes a diagnosis of Von Willebrand's disease less likely and points toward an autoimmune cause of this patient's symptoms.

   Discuss (6) Improve

Next question >

Abnormal coagulation ★

Cause	Factors affected
Heparin	Prevents activation factors 2,9,10,11
Warfarin	Affects synthesis of factors 2,7,9,10
DIC	Factors 1,2,5,8,11
Liver disease	Factors 1,2,5,7,9,10,11

Interpretation blood clotting test results


Disorder	APTT	PT	Bleeding time
Haemophilia	Increased	Normal	Normal
von Willebrand's disease	Increased	Normal	Increased
Vitamin K deficiency	Increased	Increased	Normal


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Next question >

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Textbooks

High-yield textbook


Extended textbook

Media



Coagulation cascade



DirtyUSMLE - YouTube


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Coagulation cascade



Handwritten Tutorials - YouTube


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Coagulation cascade

KhanAcademy - YouTube

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[Report broken media](#)

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A 65-year-old female, known to have metastatic breast carcinoma presents to the hospital with a 24-hour history of increasing pain, swelling and erythema of her right calf. She is otherwise relatively well. She was diagnosed with breast carcinoma four years previously and was initially treated with surgery, radiotherapy and chemotherapy. She was found to have disease recurrence with distant metastasis 12 months previously. She is known to have liver and bone metastases.

On examination, she appears pale and has some hair loss following recent chemotherapy. Apart from her swollen, erythematous, tender right calf and a fentanyl patch examination is unremarkable.

Bloods on admission show:

Hb	100 g/l
Platelets	$180 \times 10^9/l$
WBC	$7.2 \times 10^9/l$
D-Dimer	1276 $\mu g/L$ (normal $<500\mu g/L$)

Na^+	132 mmol/l
K^+	4.5 mmol/l
Urea	7.2mmol/l
Creatinine	110 $\mu mol/l$

She is diagnosed with a right leg deep vein thrombosis. Given her current clinical condition, what is the best method of anticoagulation?

- ☐ Low molecular weight heparin (LMWH) and warfarin until warfarin therapeutic followed by warfarin therapy for 6 months then reassess. ×
- ☐ Low molecular weight heparin (LMWH) for 3-6 months then reassess ×
- ☐ Warfarin therapy starting with a slow loading regime for 6 months then reassess ×
- ☐ Direct oral anticoagulants (DOACs) for 3-6 months then reassess ×
- ☐ Referral for inferior vena cava filter insertion ×

Submit answer

Reference ranges 

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A 65-year-old female, known to have metastatic breast carcinoma presents to the hospital with a 24-hour history of increasing pain, swelling and erythema of her right calf. She is otherwise relatively well. She was diagnosed with breast carcinoma four years previously and was initially treated with surgery, radiotherapy and chemotherapy. She was found to have disease recurrence with distant metastasis 12 months previously. She is known to have liver and bone metastases.

On examination, she appears pale and has some hair loss following recent chemotherapy. Apart from her swollen, erythematous, tender right calf and a fentanyl patch examination is unremarkable.

Bloods on admission show:

Hb	100 g/l
Platelets	180 * 10 ⁹ /l
WBC	7.2* 10 ⁹ /l
D-Dimer	1276 µg/L (normal <500µg/L)

Na ⁺	132 mmol/l
K ⁺	4.5 mmol/l
Urea	7.2mmol/l
Creatinine	110 µmol/l

She is diagnosed with a right leg deep vein thrombosis. Given her current clinical condition, what is the best method of anticoagulation?

Low molecular weight heparin (LMWH) and warfarin until warfarin therapeutic followed by warfarin therapy for 6 months then reassess.	5%
Low molecular weight heparin (LMWH) for 3-6 months then reassess	9%
Warfarin therapy starting with a slow loading regime for 6 months then reassess	1%
Direct oral anticoagulants (DOACs) for 3-6 months then reassess	84%
Referral for inferior vena cava filter insertion	2%



Discuss (3)

Improve

Next question >

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1

Clinical feature	Points
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

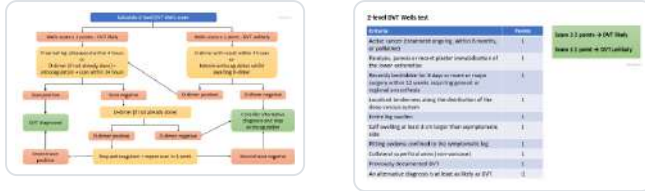
- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)
 - interim therapeutic anticoagulation used to mean giving low-molecular weight heparin
 - NICE updated their guidance in 2020. They now recommend using an anticoagulant that can be continued if the result is positive.
 - this means normally a direct oral anticoagulant (DOAC) such as apixaban or rivaroxaban
- if the scan is negative but the D-dimer is positive:
 - stop interim therapeutic anticoagulation
 - offer a repeat proximal leg vein ultrasound scan 6 to 8 days later

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test
 - this should be done within 4 hours. If not, interim therapeutic anticoagulation should be given until the result is available
 - if the result is negative then DVT is unlikely and alternative diagnoses should be considered
 - if the result is positive then a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if a proximal leg vein ultrasound scan cannot be carried out within 4 hours interim therapeutic anticoagulation should be administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

D-dimer tests

- NICE recommend either a point-of-care (finger prick) or laboratory-based test
- age-adjusted cut-offs should be used for patients > 50 years old



Management

The cornerstone of VTE management is anticoagulant therapy. This was historically done with warfarin, often preceded by heparin until the INR was stable. However, the development of DOACs, and an evidence base supporting their efficacy, has changed modern management.

Choice of anticoagulant

- the big change in the 2020 guidelines was the increased use of DOACs
- apixaban or rivaroxaban (both DOACs) should be offered first-line following the diagnosis of a DVT
 - instead of using low-molecular weight heparin (LMWH) until the diagnosis is confirmed, NICE now advocate using a DOAC once a diagnosis is suspected, with this continued if the diagnosis is confirmed
 - if neither apixaban or rivaroxaban are suitable then either LMWH followed by dabigatran or edoxaban OR LMWH followed by a vitamin K antagonist (VKA, i.e. warfarin)
- if the patient has active cancer
 - previously LMWH was recommended
 - the new guidelines now recommend using a DOAC, unless this is contraindicated
- if renal impairment is severe (e.g. $< 15/\text{min}$) then LMWH, unfractionated heparin or LMWH followed by a VKA
- if the patient has antiphospholipid syndrome (specifically 'triple positive' in the guidance) then LMWH followed by a VKA should be used

Length of anticoagulation

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer at increased risk
 - an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding

- the ORBIT score can be used to help assess the risk of bleeding
- NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



+

Q

123



Next question >

B

I



A



Textbooks

High-yield textbook

Extended textbook

Links

NICE

👍 5 👎 0

[2020 Venous thromboembolism guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Deep vein thrombosis](#)



Osmosis - YouTube

👍 3 👎 0



Understanding Deep Vein Thrombosis (DVT)

Zero To Finals - YouTube

 2  1


























Deep Vein Thrombosis - Overview (pathophysiology, treatment, complications)

Armando Hasudungan - YouTube

 3  2

[Report broken media](#)

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A 68-year-old woman is reviewed in haematology clinic routinely. She has a past medical history of chronic lymphocytic leukaemia (CLL), characterised by a deletion of the short arm of chromosome 17 (17p).

On examination, there is cervical lymphadenopathy and splenomegaly.

Blood tests:

Hb	115 g/L	Male: (135-180) Female: (115 - 160)
Platelets	$189 \times 10^9/L$	(150 - 400)
WBC	$35.3 \times 10^9/L$	(4.0 - 11.0)
Neuts	$2.1 \times 10^9/L$	(2.0 - 7.0)
Lymphs	$33.0 \times 10^9/L$	(1.0 - 3.5)
Mono	$0.2 \times 10^9/L$	(0.2 - 0.8)
Eosin	$0.0 \times 10^9/L$	(0.0 - 0.4)
Na ⁺	138 mmol/L	(135 - 145)
K ⁺	4.2 mmol/L	(3.5 - 5.0)
Urea	5.1 mmol/L	(2.0 - 7.0)
Creatinine	88 $\mu\text{mol/L}$	(55 - 120)
CRP	4 mg/L	(< 5)
Lactate dehydrogenase (LDH)	180 U/L	(140-280)

Given the clinical history and underlying diagnosis, which clinical feature is associated with the worst prognosis?

- ☐ Female sex ×
- ☐ Age > 60 ×
- ☐ Lymphocyte count > 30 ×
- ☐ Normal LDH ×
- ☐ 17p deletion ×

Submit answer

Reference ranges 

Score: **18%**

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Na ⁺	138 mmol/L	(135 - 145)
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Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Lactate dehydrogenase (LDH)	180 U/L	(140-280)

Given the clinical history and underlying diagnosis, which clinical feature is associated with the worst prognosis?

Female sex	2%
Age > 60	8%
Lymphocyte count > 30	5%
Normal LDH	1%
17p deletion	84%

del 17p is associated with a poor prognosis in CLL

Important for me Less important

17p deletion is the correct answer. The patient has chronic lymphocytic leukaemia. This is a type of cancer in which the bone marrow makes too many lymphocytes, as evidenced in this case. The cancer in this case is characterized by a genetic mutation causing deletion of 17p, which is a part of chromosome 17. This is associated with a poor prognosis in CLL. It is seen in 5-10% of patients. The absence of part of chromosome 17 results in absence of one allele of the TP53 tumour suppressor gene, predisposing to the development of CLL.

Age > 60 is incorrect. Poor prognosis is associated with those > 70 years of age.

Lymphocyte count > 30 is incorrect. Poor prognosis is associated with those patients with lymphocyte counts > 50.

Normal LDH is incorrect. A raised LDH implies a worse prognosis.

Female sex is incorrect. Male sex implies a worse prognosis.



Discuss (1)

Improve

Next question >

Chronic lymphocytic leukaemia: prognostic factors ★

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive
- TP53 mutation

Chromosomal changes

- deletion of the long arm of chromosome 13 (del 13q) is the most common abnormality, being seen in around 50% of patients. It is associated with a **good** prognosis
- deletions of part of the short arm of chromosome 17 (del 17p) are seen in around 5-10% of patients and are associated with a **poor** prognosis



123

[Next question >](#)**B***I***A****T**

Textbooks

[High-yield textbook](#)[Extended textbook](#)

Links

[British Committee for Standards in Haematology](#)

2



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[2012 CLL guidelines](#)[Suggest link](#)[Report broken link](#)

Media

[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)[Medicosis Perfectionalis - YouTube](#)

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Question 81 of 89



A 24-year-old woman is admitted with a 1-hour history of worsening dyspnoea. On examination, you note stridor and marked angioedema of the lips and tongue. No rash is present. You immediately seek the assistance of the anaesthetic team to help secure the airway.

The patient has a history of hereditary angioedema. You are told that due to manufacturing issues, IV C1-inhibitor concentrate is not available.

What alternative treatment should be offered?

- | | |
|--|---|
| <input type="radio"/> Danazol | × |
| <input type="radio"/> Fresh frozen plasma | × |
| <input type="radio"/> Intramuscular adrenaline | × |
| <input type="radio"/> Intravenous methylprednisolone | × |
| <input type="radio"/> Tranexamic acid | × |

Submit answer

Reference ranges 

Score: **18%**

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A 24-year-old woman is admitted with a 1-hour history of worsening dyspnoea. On examination, you note stridor and marked angioedema of the lips and tongue. No rash is present. You immediately seek the assistance of the anaesthetic team to help secure the airway.

The patient has a history of hereditary angioedema. You are told that due to manufacturing issues, IV C1-inhibitor concentrate is not available.

What alternative treatment should be offered?

Danazol	17%
Fresh frozen plasma	63%
Intramuscular adrenaline	9%
Intravenous methylprednisolone	5%
Tranexamic acid	5%

Hereditary angioedema: the acute management is IV C1-inhibitor concentrate or fresh frozen plasma if this is not available

Important for me Less important





The correct answer is **fresh frozen plasma**. This is considered a second-line therapy where C1 inhibitor concentrate is not available as the plasma itself contains C1 inhibitor. No randomised control trials exist but a majority of case reports describe efficacy with signs of improvement described between 30 minutes and 12 hours.

Danazol is incorrect. This is a synthetic androgen that is used in prophylaxis of acute episodes in patients with hereditary angioedema. It has not been shown to provide any benefit in acute attacks.

Intramuscular adrenaline is incorrect. Similar to glucocorticoids, adrenaline is not effective in hereditary angioedema. Episodes of angioedema not responding to adrenaline may be one of the first clues to the diagnosis.

Intravenous methylprednisolone is incorrect. While glucocorticoids are used in histamine-driven angioedema, they are not effective in hereditary angioedema as the pathogenesis is driven by bradykinin rather than histamine.

Tranexamic acid is incorrect. It has been used for prophylaxis but a minimal effect is seen when used for the treatment of acute attacks.

   Discuss (1)  Improve

Next question >

Hereditary angioedema ★

Hereditary angioedema (HAE) is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH, C1 esterase inhibitor) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

Symptoms









- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

Management

- **acute**
 - HAE does not respond to adrenaline, antihistamines, or glucocorticoids
 - IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help



Next question >

B *I*  **A** ▼    ▼  ▼  ▼  

Textbooks

High-yield textbook

Extended textbook

Links

Patient.info

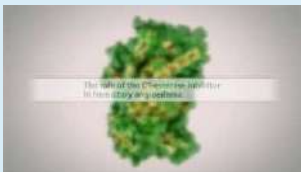
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[Hereditary angioedema review](#)

[Suggest link](#)

[Report broken link](#)

Media



[The Role of the C1-Esterase Inhibitor in HAE](#)

Individual - YouTube

👍 3 👎 0

[Report broken media](#)

Score: **20.2%**

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A 35-year-old woman presents to the emergency department with a one day history of a fever. She has a past medical history of metastatic breast cancer and has received her most recent round of chemotherapy 8 days ago. She is not on any other regular medications.

Her observations are heart rate 111 beats per minute, blood pressure 96/58 mmHg, respiratory rate 22/minute, oxygen saturations 97% on room air and temperature 38.7°C.

On examination, she is warm to touch with capillary refill time < 2 seconds. A bounding pulse is noted. There is no obvious localizing source of infection from the rest of the examination.



Urinalysis is unremarkable.

Plain radiography of the chest is normal.

Blood tests:

Hb	121 g/L	Male: (135-180) Female: (115 - 160)
Platelets	389 * 10 ⁹ /L	(150 - 400)
WBC	1.7 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	0.4 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	0.9 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.2 * 10 ⁹ /L	(0.0 - 0.4)
Na ⁺	137 mmol/L	(135 - 145)
K ⁺	4.4 mmol/L	(3.5 - 5.0)
Bicarbonate	20 mmol/L	(22 - 29)
Urea	8.9 mmol/L	(2.0 - 7.0)
Creatinine	111 µmol/L	(55 - 120)
CRP	180mg/l	(<4)

What is the appropriate antibiotic choice?

- ☐ Meropenem
 
- ☐ Piperacillin/tazobactam
 

- ☐ Piperacillin/tazobactam and gentamicin ×
- ☐ Piperacillin/tazobactam and gentamicin and vancomycin ×
- ☐ Piperacillin/tazobactam and vancomycin ×

Submit answer

Reference ranges ▾

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A 35-year-old woman presents to the emergency department with a one day history of a fever. She has a past medical history of metastatic breast cancer and has received her most recent round of chemotherapy 8 days ago. She is not on any other regular medications.

Her observations are heart rate 111 beats per minute, blood pressure 96/58 mmHg, respiratory rate 22/minute, oxygen saturations 97% on room air and temperature 38.7°C.

On examination, she is warm to touch with capillary refill time < 2 seconds. A bounding pulse is noted. There is no obvious localizing source of infection from the rest of the examination.

Urinalysis is unremarkable.

Plain radiography of the chest is normal.

Blood tests:

Hb	121 g/L	Male: (135-180) Female: (115 - 160)
Platelets	389 * 10 ⁹ /L	(150 - 400)
WBC	1.7 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	0.4 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	0.9 * 10 ⁹ /L	(1.0 - 3.5)
Mono	0.2 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.2 * 10 ⁹ /L	(0.0 - 0.4)
Na ⁺	137 mmol/L	(135 - 145)
K ⁺	4.4 mmol/L	(3.5 - 5.0)
Bicarbonate	20 mmol/L	(22 - 29)
Urea	8.9 mmol/L	(2.0 - 7.0)
Creatinine	111 µmol/L	(55 - 120)
CRP	180mg/l	(<4)

What is the appropriate antibiotic choice?

Meropenem

2%

Piperacillin/tazobactam

78%

Piperacillin/tazobactam and gentamicin

13%

Piperacillin/tazobactam and gentamicin and vancomycin

2%

Piperacillin/tazobactam and vancomycin

5%

Piperacillin with tazobactam (Tazocin) is the empirical antibiotic of choice for neutropenic sepsis

Important for me Less important

Piperacillin/tazobactam is the correct answer. This patient has neutropenic sepsis secondary to chemotherapy treatment. This choice is supported by NICE guidelines and is first-line for the treatment of neutropenic sepsis.

Meropenem is incorrect. If the patient fails to respond after 48 hours then they may be escalated to meropenem.

Piperacillin/tazobactam and vancomycin is incorrect. Some units advocate giving vancomycin in addition to piperacillin/tazobactam if there is an indwelling central venous access device. This patient does not have such a device in situ and this procedure is not supported by NICE.

Piperacillin/tazobactam and gentamicin is incorrect. NICE specifically advise not adding an aminoglycoside unless local policy dictates.

Piperacillin/tazobactam and gentamicin and vancomycin is incorrect. This is not a treatment strategy supported by NICE.



Discuss (4)

Improve

Next question >

Neutropenic sepsis ★

Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of $< 0.5 \times 10^9$ in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis

Aetiology

- coagulase-negative, Gram-positive bacteria are the most common cause, particularly *Staphylococcus epidermidis*
 - this is probably due to the use of indwelling lines in patients with cancer

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of $< 0.5 \times 10^9$ as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommends starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients



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Next question >

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Textbooks

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Extended textbook

Links

NICE

👍 3 👎 1

[2012 Neutropenic sepsis guidelines](#)

Christies

👍 2 👎 4

[2013 Neutropenic sepsis guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Febrile Neutropenia](#)

Townsend Teaching - YouTube

👍 1 👎 0



[What is febrile neutropaenia \(neutropenia\)? - neutrophil function, pathophysiology, treatment](#)

Armando Hasudungan - YouTube

👍 2 👎 1



[Neutropenic sepsis](#)

Oncology for Medical Students - YouTube

👍 5 👎 3

[Report broken media](#)

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A 67-year-old woman presents to her GP with a lump in her armpit that she first noticed two months ago, and feels is getting bigger. She has not suffered from pyrexia, night sweats, weight loss or lethargy. The GP runs some blood tests, which can be seen below.

Hb	116 g/L	Male: (135-180) Female: (115 - 160)
Platelets	160 * 10 ⁹ /L	(150 - 400)
WBC	72 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	5 * 10 ⁹ /L	(2.0 - 7.0)
Lymphocytes	66 * 10 ⁹ /L	(1.0 - 3.5)
Blood film	smudge cells	

Which of the following would imply a poor prognosis in this woman?

- ☐ Female sex ×
- ☐ Philadelphia translocation ×
- ☐ Low B2-microglobulin ×
- ☐ Del 17p ×
- ☐ Age less than 70 ×

Submit answer

Reference ranges 

Score: **18%**

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Neuts	5 * 10 ⁹ /L	(2.0 - 7.0)
Lymphocytes	66 * 10 ⁹ /L	(1.0 - 3.5)
Blood film	smudge cells	

Which of the following would imply a poor prognosis in this woman?

Female sex	3%
Philadelphia translocation	13%
Low B2-microglobulin	5%
Del 17p	77%
Age less than 70	2%

del 17p is associated with a poor prognosis in CLL

Important for me Less important

This woman is suffering from chronic lymphocytic leukaemia (CLL), a slowly progressive disease. Most patients are either asymptomatic or present with lymphadenopathy. Only 10% of patients will have B symptoms of lymphoma. Half of the patients present with splenomegaly and about 15% with hepatomegaly. The key to making this diagnosis is the lymphocyte-predominant leukocytosis, with smudge cells on the blood film. Smudge cells, also known as smear cells, are cell remnants that arise during slide preparation and are the result of abnormally fragile lymphocytes in CLL.

From the options given above, the only poor prognostic indicator is del 17p mutation, which indicates resistance to standard chemotherapy regimens.

B2-microglobulin levels are used in multiple myeloma where raised levels imply poor prognosis. It has also been included in the new (2016) CLL international prognostic index, where again high levels imply poor prognosis.

Philadelphia translocation, t(9;22), is a poor prognostic factor in ALL.

Male sex, not female sex, is a poor prognostic factor.

An age of fewer than 70 years old is a good prognostic marker.

   Discuss (4)

Improve

[Next question >](#)

Chronic lymphocytic leukaemia: prognostic factors ★

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive
- TP53 mutation

Chromosomal changes

- deletion of the long arm of chromosome 13 (del 13q) is the most common abnormality, being seen in around 50% of patients. It is associated with a **good** prognosis
- deletions of part of the short arm of chromosome 17 (del 17p) are seen in around 5-10% of patients and are associated with a **poor** prognosis

[Next question >](#)

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Textbooks

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Links

British Committee for Standards in Haematology

 2  0

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media














[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)

Medicosis Perfectionalis - YouTube

 3  0

[Report broken media](#)

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A 16-year-old boy from Iran presents to the emergency department with dyspnoea, dry cough, and fevers.

On arrival, his oxygen saturations are 91% with a respiratory rate of 27/minute. His blood pressure is 110/70mmHg and heart rate 89/minute. There are widespread crackles on auscultation.

Chest x-ray shows diffuse bilateral interstitial infiltrates. You begin treatment for community-acquired pneumonia and send sputum samples for culture.

Blood tests:

Hb	95g/L	Male: (135-180) Female: (115 - 160)
Platelets	140* 10 ⁹ /L	(150 - 400)
WBC	2.7* 10 ⁹ /L	(4.0 - 11.0)
Neuts	0.7* 10 ⁹ /L	(2.0 - 7.0)
Lymphs	1.7* 10 ⁹ /L	(1.0 - 3.5)
Mono	0.1* 10 ⁹ /L	(0.2 - 0.8)
Eosin	0.2* 10 ⁹ /L	(0.0 - 0.4)
Na ⁺	140mmol/L	(135 - 145)
K ⁺	3.8mmol/L	(3.5 - 5.0)
Urea	9mmol/L	(2.0 - 7.0)
Creatinine	80µmol/L	(55 - 120)
CRP	234mg/L	(< 5)

His sputum sample grows *Pneumocystis jirovecii* and his antimicrobials are changed to include Co-trimoxazole.

You return to take a more detailed history. He denies any recent treatment with glucocorticoids or immunosuppressive agents. He denies intravenous drug use and informs you he is not yet sexually active. His mother is in attendance and tells you he has suffered from recurrent gastroenteritis throughout his childhood and she feels this led to him being smaller than his peers.

What is the most likely underlying unifying diagnosis?

☐ *Cryptosporidium*



<input type="radio"/>	Hyper IgM syndrome	×
<input type="radio"/>	HIV	×
<input type="radio"/>	Acute lymphoblastic leukaemia	×
<input type="radio"/>	Malnutrition	×

Submit answer

Reference ranges ▾

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You return to take a more detailed history. He denies any recent treatment with glucocorticoids or immunosuppressive agents. He denies intravenous drug use and informs you he is not yet sexually active. His mother is in attendance and tells you he has suffered from recurrent gastroenteritis throughout his childhood and she feels this led to him being smaller than his peers.

What is the most likely underlying unifying diagnosis?

Hyper IgM syndrome	80%
HIV	8%
Acute lymphoblastic leukaemia	7%
Malnutrition	3%

Hyper IgM syndrome characteristically presents with infections e.g. *Pneumocystis* pneumonia, hepatitis, diarrhoea

Important for me Less important

This patient has presented with pneumocystis pneumonia, an opportunistic infection caused by an underlying immune deficiency (hyper IgM syndrome).

Hyper IgM syndrome is a heterogeneous group of disorders characterised by defective class-switch recombination leading to raised serum IgM with low levels of IgG and IgA. The most common form is an X-linked recessive trait due to mutation of CD40LG gene affecting roughly 2/1,000,000 males. The mechanism involves impaired immune signalling between T and B cells leading to primary immune deficiency.

Hyper IgM typically presents in infancy as acute severe infection such as pneumocystis pneumonia or cryptosporidium. It may also present as chronic infections throughout childhood with failure to thrive. CMV is common and may lead to associated liver disease. It is also associated with increased risk of hepatocellular carcinoma, cholangiocarcinoma and neuroectodermal tumours. A minority of patients may present with autoimmune disease such as inflammatory bowel disease.

Acute lymphoblastic leukaemia is unlikely given the long history of recurrent infection.

HIV is less likely as this patient denies any risk factors or exposure.

Cryptosporidium is an opportunistic infection and is commonly associated with hyper IgM syndrome. It is the likely causative organism for his recurrent gastroenteritis but does not explain his current presentation. Given the history of opportunistic infections, he should be investigated for causes of immunodeficiency.

Malnutrition is incorrect. Recurrent gastroenteritis in childhood may lead to malnutrition and secondary immunodeficiency. However, the question asks for an 'underlying unifying diagnosis'. This should include a cause for his history of recurrent gastroenteritis.



 Discuss (2)
 Improve

Next question >

Primary immunodeficiency ★

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
Chronic granulomatous disease	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. <i>Staphylococcus aureus</i>) and fungi (e.g. <i>Aspergillus</i>) Negative nitroblue-tetrazolium test Abnormal dihydrorhodamine flow cytometry test
Chediak-Higashi syndrome	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen Giant granules in neutrophils and platelets
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen Absence of neutrophils/pus at sites of infection

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Low antibody levels, specifically in immunoglobulin (Ig) types IgG, IgM and IgA. Recurrent chest infections. May also predispose to autoimmune disorders and lymphoma

Disorder	Underlying defect	Notes
Bruton's (x-linked) congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen Absence of B-cells with reduced immunoglobulins of all classes
<u>Selective immunoglobulin A deficiency</u>	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and respiratory infections Associated with coeliac disease and may cause false negative coeliac antibody screen Severe reactions to blood transfusions may occur (anti-IgA antibodies → anaphylaxis)

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4th pharyngeal pouches	Common features include congenital heart disease (e.g. tetralogy of Fallot), learning difficulties, hypocalcaemia, recurrent viral/fungal diseases, cleft palate

Combined B- and T-cell disorders

Disorder	Underlying defect	Notes
<u>Severe combined immunodeficiency</u>	Many varying causes. Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. Other causes include adenosine deaminase deficiency	Recurrent infections due to viruses, bacteria and fungi. Reduced T-cell receptor excision circles Stem cell transplantation may be successful

Disorder	Underlying defect	Notes
Ataxic telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia (spider angiomas), recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopaenia. Low IgM levels Increased risk of autoimmune disorders and malignancy
Hyper IgM Syndromes	Mutations in the CD40 gene	Infection/ <i>Pneumocystis</i> pneumonia, hepatitis, diarrhoea

Next question >

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Textbooks

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Media



X linked agammaglobulinemia (Bruton agammaglobulinemia)

Osmosis - YouTube

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Well defined genetic immunodeficiency - DiGeorge Syndrome and Job Syndrome

Armando Hasudungan - YouTube

👍 4 👎 1



Leukocyte adhesion deficiency

Osmosis - YouTube

👍 4 👎 1



Selective immunoglobulin A deficiency

Osmosis - YouTube

👍 2 👎 1



Primary antibody deficiency - Common Variable Immunodeficiency (CVID) , X-linked agammaglobulinemia

Armando Hasudungan - YouTube

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Digeorge syndrome (22q11.2 deletion syndrome)

Osmosis - YouTube

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Question 85 of 89



A 72-year-old woman presents to the emergency department with a painful and swollen leg. This has developed over two days, and she otherwise feels well in herself. She was recently away on holiday to Spain and returned four weeks ago. She is able to mobilise independently and has had no reduced periods of mobility. She has a background breast cancer diagnosed four years ago, which unfortunately relapsed and spread into her liver. She is now on hormonal treatment only.

On examination, her left leg is swollen and red, and the calf diameter is significantly larger on the left side. A doppler ultrasound scan demonstrates a left-sided deep vein thrombus. What is the most appropriate anticoagulation strategy?

- ☐ 2-4 months of low molecular weight heparin (LMWH) ×
- ☐ 3-6 months of low molecular weight heparin (LMWH) ×
- ☐ 3-6 months of a direct oral anticoagulant (DOAC) ×
- ☐ Three months of warfarin ×
- ☐ Six months of warfarin ×

Submit answer

Reference ranges 

Score: **18%**

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Question 85 of 89



A 72-year-old woman presents to the emergency department with a painful and swollen leg. This has developed over two days, and she otherwise feels well in herself. She was recently away on holiday to Spain and returned four weeks ago. She is able to mobilise independently and has had no reduced periods of mobility. She has a background breast cancer diagnosed four years ago, which unfortunately relapsed and spread into her liver. She is now on hormonal treatment only.

On examination, her left leg is swollen and red, and the calf diameter is significantly larger on the left side. A doppler ultrasound scan demonstrates a left-sided deep vein thrombus. What is the most appropriate anticoagulation strategy?

- | | |
|---|-----|
| 2-4 months of low molecular weight heparin (LMWH) | 1% |
| 3-6 months of low molecular weight heparin (LMWH) | 7% |
| 3-6 months of a direct oral anticoagulant (DOAC) | 89% |
| Three months of warfarin | 1% |
| Six months of warfarin | 2% |

Cancer patients with VTE - 6 months of a DOAC

Important for me Less important

NICE updated their guidelines in 2020. DOACs are now preferred to LMWH for patients with active cancer.

As active cancer is likely to cause a continued pro-coagulopathic state, it is recommended to continue anticoagulation for longer than the standard 3 months.



Discuss (3)

Improve

Next question >

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

- if the scan is negative but the D-dimer is positive:

- perform a D-dimer test

- if the result is negative then DVT is unlikely and alternative diagnoses should be considered

- NICE recommend either a point-of-care (finger prick) or laboratory-based test
- age-adjusted cut-offs should be used for patients > 50 years old



The cornerstone of VTE management is anticoagulant therapy. This was historically done with warfarin, often preceded by heparin until the INR was stable. However, the development of DOACs, and an evidence base supporting their efficacy, has changed modern management.

- the big change in the 2020 guidelines was the increased use of DOACs
- apixaban or rivaroxaban (both DOACs) should be offered first-line following the diagnosis of a DVT
 - instead of using low-molecular weight heparin (LMWH) until the diagnosis is confirmed, NICE now advocate using a DOAC once a diagnosis is suspected, with this continued if the diagnosis is confirmed

- if neither apixaban or rivaroxaban are suitable then either LMWH followed by dabigatran or edoxaban OR LMWH followed by a vitamin K antagonist (VKA, i.e. warfarin)
- if the patient has active cancer
 - previously LMWH was recommended
 - the new guidelines now recommend using a DOAC, unless this is contraindicated
- if renal impairment is severe (e.g. $< 15/\text{min}$) then LMWH, unfractionated heparin or LMWH followed by a VKA
- if the patient has antiphospholipid syndrome (specifically 'triple positive' in the guidance) then LMWH followed by a VKA should be used

Length of anticoagulation

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer at increased risk
 - an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



123



Next question >

B

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A



T



Textbooks

High-yield textbook

Extended textbook

Links

NICE

👍 5 🗑 0

[2020 Venous thromboembolism guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Deep vein thrombosis](#)

Osmosis - YouTube

👍 3 🗑 0



[Understanding Deep Vein Thrombosis \(DVT\)](#)

Zero To Finals - YouTube

👍 2 🗑 1



[Deep Vein Thrombosis - Overview \(pathophysiology, treatment, complications\)](#)

Armando Hasudungan - YouTube

👍 3 🗑 2

[Report broken media](#)

Score: **20.2%**

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89	✗



A 52-year-old woman presents to her GP complaining of fatigue and bruising. She has no significant medical co-morbidities. She is referred to the haematology clinic after an abnormal full blood count. Blood results are as follows:

Hb	112 g/L	Male: (135 - 180) Female: (115 - 160)
Platelets	$150 \times 10^9/\text{L}$	(150 - 400)
WBC	$25.3 \times 10^9/\text{L}$	(4.0 - 11.0)
Neuts	$4.0 \times 10^9/\text{L}$	(2.0 - 7.0)
Lymphs	$16.2 \times 10^9/\text{L}$	(1.0 - 3.5)
Mono	$3.0 \times 10^9/\text{L}$	(0.2 - 0.8)
Eosin	$1.1 \times 10^9/\text{L}$	(0.0 - 0.4)

LDH	250 U/L	(140 - 280 U/L)
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Multicolour flow cytometry assay reports CD20+, CD23+, and CD5+ expression. She also undergoes fluorescence in situ hybridization (FISH) which reveals a deletion in the short arm of chromosome 17.

Which of the following features in this case is associated with a poor prognosis?

<input type="radio"/>	Age	×
<input type="radio"/>	FISH result	×
<input type="radio"/>	Flow cytometry assay result	×
<input type="radio"/>	Gender	×
<input type="radio"/>	LDH level	×

Submit answer

Reference ranges

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Question 86 of 89



A 52-year-old woman presents to her GP complaining of fatigue and bruising. She has no significant medical co-morbidities. She is referred to the haematology clinic after an abnormal full blood count. Blood results are as follows:

Hb	112 g/L	Male: (135 - 180) Female: (115 - 160)
Platelets	150 * 10 ⁹ /L	(150 - 400)
WBC	25.3 * 10 ⁹ /L	(4.0 - 11.0)
Neuts	4.0 * 10 ⁹ /L	(2.0 - 7.0)
Lymphs	16.2 * 10 ⁹ /L	(1.0 - 3.5)
Mono	3.0 * 10 ⁹ /L	(0.2 - 0.8)
Eosin	1.1 * 10 ⁹ /L	(0.0 - 0.4)

LDH	250 U/L	(140 - 280 U/L)
-----	---------	-----------------

Multicolour flow cytometry assay reports CD20+, CD23+, and CD5+ expression. She also undergoes fluorescence in situ hybridization (FISH) which reveals a deletion in the short arm of chromosome 17.

Which of the following features in this case is associated with a poor prognosis?

Age	5%
FISH result	68%
Flow cytometry assay result	19%
Gender	5%
LDH level	4%

del 17p is associated with a poor prognosis in CLL

Important for me Less important

The high white cell count composed mostly of lymphocytes points towards a diagnosis of chronic lymphocytic leukaemia (CLL). In CLL, deletion (del) of the short arm of chromosome 17 (17p) is found in under 10% of patients. This abnormality is associated with rapid progression of the



disease, as well as a poor response to treatment strategies.

Prognosis is less favourable in those who are over the age of 70, rather than younger patients like this one.

CD20+, CD23+, and CD5+ are surface antigens that are expressed in most CLL cases and shouldn't affect prognosis.

Male sex, rather than female sex, is associated with a poor prognosis in CLL.

Raised LDH is a marker for poor prognostic outcome, but it is normal in her case.

   Discuss (4) [Improve](#)

[Next question >](#)

Chronic lymphocytic leukaemia: prognostic factors ★




Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive
- TP53 mutation

Chromosomal changes

- deletion of the long arm of chromosome 13 (del 13q) is the most common abnormality, being seen in around 50% of patients. It is associated with a **good** prognosis
- deletions of part of the short arm of chromosome 17 (del 17p) are seen in around 5-10% of patients and are associated with a **poor** prognosis

[Next question >](#)

B *I*  **A** ▼    ▼ **T** ▼  ▼  

Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

👍 2 👎 0

[2012 CLL guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Chronic Lymphocytic Leukemia \(CLL\) - Diagnosis & Treatment](#)

Medicosis Perfectionalis - YouTube

👍 3 👎 0

[Report broken media](#)

Score: **20.2%**

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An 18-year-old woman attends the emergency department with difficulty breathing.

On examination, she is cyanosed, her oxygen saturations are 84% on a finger probe, and her chest is clear.

She tells you that she has had a blue tinge around her mouth for her whole life and that she did have some investigations abroad before moving to the UK aged 4.

You take a blood gas, the sample is a dark brown colour. The results are as follows:

pH	7.35	7.35-7.45
PaCO ₂	4.5kPa	4.7 - 6.0
PaO ₂	12kPa	11 - 13

Given the likely diagnosis, what is the treatment of choice for the underlying condition?

- ☐ 15L oxygen via a non-rebreathe mask ×
- ☐ Ascorbic acid ×
- ☐ Hyperbaric oxygen ×
- ☐ IV methylthioninium chloride ×
- ☐ Nitric oxide ×

Submit answer

Reference ranges 

Score: **18%**

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Question 87 of 89



An 18-year-old woman attends the emergency department with difficulty breathing.

On examination, she is cyanosed, her oxygen saturations are 84% on a finger probe, and her chest is clear.

She tells you that she has had a blue tinge around her mouth for her whole life and that she did have some investigations abroad before moving to the UK aged 4.

You take a blood gas, the sample is a dark brown colour. The results are as follows:

pH	7.35	7.35-7.45
PaCO ₂	4.5kPa	4.7 - 6.0
PaO ₂	12kPa	11 - 13

Given the likely diagnosis, what is the treatment of choice for the underlying condition?

15L oxygen via a non-rebreathe mask	2%
Ascorbic acid	71%
Hyperbaric oxygen	3%
IV methylthioninium chloride	24%
Nitric oxide	1%

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency

Important for me Less important

The chocolate brown blood sample, normal PaO₂ but low oxygen saturations, and persistent cyanosis since childhood all point towards methaemoglobinaemia. Congenital NADH methaemoglobinaemia reductase deficiency is usually diagnosed in childhood presenting with persistent cyanosis with or without shortness of breath.




Ascorbic acid is the correct answer, it is the treatment of choice for NADH methaemoglobinaemia reductase deficiency.

15L oxygen via a non-rebreathe mask is incorrect. This patient may very well have 15L oxygen via a non-rebreathe mask applied in the emergency setting due to the low oxygen saturations, but this would not be the treatment for the underlying condition.

Hyperbaric oxygen is incorrect, this would be a treatment option for carbon monoxide poisoning.

IV methylthioninium chloride is incorrect, it would be the treatment of choice for acquired methaemoglobinaemia rather than congenital.

Nitric oxide is incorrect, this is actually a cause of acquired methaemoglobinaemia.

		 Discuss (2)	Improve
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Next question >

Methaemoglobinaemia ★

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe^{2+} to Fe^{3+} . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe^{3+} cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes

- drugs: sulphonamides, nitrates (including recreational nitrates e.g. amyl nitrite 'poppers'), dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO_2 but decreased oxygen saturation

Management

- NADH methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylthioninium chloride (methylene blue) if acquired



123

[Next question >](#)**B***I***A****T**

Textbooks

[High-yield textbook](#)[Extended textbook](#)

Links

[Life in the Fast Lane](#)

6



3

[Methaemoglobinaemia](#)[The Internet Book of Critical Care](#)

10



4

[Methemoglobinemia](#)[Suggest link](#)[Report broken link](#)

Media

[Methaemoglobinaemia](#)[Osmosis - YouTube](#)

7



2

[Report broken media](#)

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Question 88 of 89



An 83-year-old woman is seen in clinic by her oncologist. She has recently been diagnosed with chronic lymphocytic leukaemia (CLL). Her blood tests and clinical picture are stable and therefore she is being monitored and treatment has not been initiated. She is to undergo genetic testing to assess her prognosis.

Which of the following is associated with a poor prognosis in her condition?

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|-------------------------------------|---|
| <input type="radio"/> IGHV mutation | × |
| <input type="radio"/> t(8;21) | × |
| <input type="radio"/> Trisomy 8 | × |
| <input type="radio"/> t(9;22) | × |
| <input type="radio"/> del 17p | × |

Submit answer

Reference ranges 

Score: **18%**

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An 83-year-old woman is seen in clinic by her oncologist. She has recently been diagnosed with chronic lymphocytic leukaemia (CLL). Her blood tests and clinical picture are stable and therefore she is being monitored and treatment has not been initiated. She is to undergo genetic testing to assess her prognosis.

Which of the following is associated with a poor prognosis in her condition?

IGHV mutation	2%
t(8;21)	3%
Trisomy 8	1%
t(9;22)	12%
del 17p	82%

del 17p is associated with a poor prognosis in CLL

Important for me Less important

In chronic lymphocytic leukaemia, del 17p is a poor prognostic factor.

IGHV is associated with a good prognosis in CLL rather than a poor one.

t(8;21) is associated with a good prognosis in acute myeloid leukaemia.

Trisomy 8 is a poor prognostic factor in acute lymphoblastic leukaemia. It is very rarely found in CLL and the prognostic relevance is unknown.

t(9;22) is the Philadelphia chromosome and is part of the diagnostic criteria for chronic myeloid leukaemia and carries a poor prognosis in acute lymphocytic leukaemia.





 Discuss

 Improve

Next question >

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive
- TP53 mutation

Chromosomal changes

- deletion of the long arm of chromosome 13 (del 13q) is the most common abnormality, being seen in around 50% of patients. It is associated with a **good** prognosis
- deletions of part of the short arm of chromosome 17 (del 17p) are seen in around 5-10% of patients and are associated with a **poor** prognosis



123



Next question >

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Textbooks

High-yield textbook

Extended textbook

Links

British Committee for Standards in Haematology

[2012 CLL guidelines](#)

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[Suggest link](#)

[Report broken link](#)

Media



Chronic Lymphocytic Leukemia (CLL) - Diagnosis & Treatment

Medicosis Perfectionalis - YouTube

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[Report broken media](#)

Score: **20.2%**

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Question 89 of 89



A 41-year-old patient receiving treatment for breast cancer presents to the Day Unit with a swollen right leg. She had a left mastectomy and axillary clearance 3 months ago and is currently receiving her second cycle of FEC (epirubicin, cyclophosphamide and fluorouracil) chemotherapy. Ultrasound doppler confirms a deep vein thrombosis of the right superficial femoral vein. The patients renal function is normal.

What is the most appropriate treatment for this patient?

- ☐ Rivaroxaban for 4-6 weeks and reassess VTE risk ×
- ☐ Warfarin for six months and reassess VTE risk ×
- ☐ Rivaroxaban for 3-6 months and reassess venous thromboembolism (VTE) risk ×
- ☐ Warfarin for 3 months and reassess VTE risk ×
- ☐ Low molecular weight heparin for for 4-6 weeks and reassess VTE risk ×

Submit answer

Reference ranges 

Score: **18%**

- 1 ×
- 2 ×
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- 8 ×
- 9 ✓

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A 41-year-old patient receiving treatment for breast cancer presents to the Day Unit with a swollen right leg. She had a left mastectomy and axillary clearance 3 months ago and is currently receiving her second cycle of FEC (epirubicin, cyclophosphamide and fluorouracil) chemotherapy. Ultrasound doppler confirms a deep vein thrombosis of the right superficial femoral vein. The patients renal function is normal.

What is the most appropriate treatment for this patient?

Rivaroxaban for 4-6 weeks and reassess VTE risk	3%
Warfarin for six months and reassess VTE risk	2%
Rivaroxaban for 3-6 months and reassess venous thromboembolism (VTE) risk	86%
Warfarin for 3 months and reassess VTE risk	3%
Low molecular weight heparin for for 4-6 weeks and reassess VTE risk	5%

Cancer patients with VTE - 6 months of a DOAC

Important for me Less important

This patient is receiving treatment for active cancer. NICE guidance recommends that patients with active cancer and venous thromboembolism (VTE) should receive 3-6 months treatment with a direct oral anticoagulant such as rivaroxaban. Their risk of further VTE should then be reassessed and a decision made by the clinical team regarding ongoing VTE treatment or prophylaxis. Previously it was recommended that low-molecular weight heparin was used in this scenario.

Warfarin is avoided in patients with active cancer due to interaction with medications; the need for treatment pauses if patients become pancytopenic and increased bleeding risk.



Discuss (3)
Improve

Deep vein thrombosis: diagnosis and management ★

NICE updated their guidelines on the investigation and management of venous thromboembolism (VTE) in 2020. Some of the key changes include recommending the following:

- the use of direct oral anticoagulants (DOACs) as first-line treatment for most people with VTE, including as interim anticoagulants before a definite diagnosis is made
- the use of DOACs in patients with active cancer, as opposed to low-molecular weight heparin as was the previous recommendation
- routine cancer screening is no longer recommended following a VTE diagnosis

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score

- DVT likely: 2 points or more
- DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if the result is positive then a diagnosis of DVT is made and anticoagulant treatment should start
 - if the result is negative a D-dimer test should be arranged. A negative scan and negative D-dimer makes the diagnosis unlikely and alternative diagnoses should be considered
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and interim therapeutic anticoagulation administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

- interim therapeutic anticoagulation used to mean giving low-molecular weight heparin
- NICE updated their guidance in 2020. They now recommend using an anticoagulant that can be continued if the result is positive.
- this means normally a direct oral anticoagulant (DOAC) such as apixaban or rivaroxaban
- if the scan is negative but the D-dimer is positive:
 - stop interim therapeutic anticoagulation
 - offer a repeat proximal leg vein ultrasound scan 6 to 8 days later

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test
 - this should be done within 4 hours. If not, interim therapeutic anticoagulation should be given until the result is available
 - if the result is negative then DVT is unlikely and alternative diagnoses should be considered
 - if the result is positive then a proximal leg vein ultrasound scan should be carried out within 4 hours
 - if a proximal leg vein ultrasound scan cannot be carried out within 4 hours interim therapeutic anticoagulation should be administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

D-dimer tests

- NICE recommend either a point-of-care (finger prick) or laboratory-based test
- age-adjusted cut-offs should be used for patients > 50 years old



Feature	Points	Score 2-3 points = DVT likely	Score 0-1 points = DVT unlikely
Active cancer (current or past, within 6 months, or unknown)	1		
Recent surgery (within 12 weeks) or trauma (within 12 weeks) or immobilisation of the lower extremities	1		
Recent hospitalisation (within 12 weeks) or major surgery (within 12 weeks) or hospital admission for medical or surgical reasons	1		
Recent travel (within 12 weeks) or long-distance travel (within 12 weeks) or long-distance travel (within 12 weeks)	1		
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Management

The cornerstone of VTE management is anticoagulant therapy. This was historically done with warfarin, often preceded by heparin until the INR was stable. However, the development of DOACs, and an evidence base supporting their efficacy, has changed modern management.

Choice of anticoagulant

- the big change in the 2020 guidelines was the increased use of DOACs
- apixaban or rivaroxaban (both DOACs) should be offered first-line following the diagnosis of a DVT
 - instead of using low-molecular weight heparin (LMWH) until the diagnosis is confirmed, NICE now advocate using a DOAC once a diagnosis is suspected, with this continued if the diagnosis is confirmed

- if neither apixaban or rivaroxaban are suitable then either LMWH followed by dabigatran or edoxaban OR LMWH followed by a vitamin K antagonist (VKA, i.e. warfarin)
- if the patient has active cancer
 - previously LMWH was recommended
 - the new guidelines now recommend using a DOAC, unless this is contraindicated
- if renal impairment is severe (e.g. $< 15/\text{min}$) then LMWH, unfractionated heparin or LMWH followed by a VKA
- if the patient has antiphospholipid syndrome (specifically 'triple positive' in the guidance) then LMWH followed by a VKA should be used

Length of anticoagulation

- all patients should have anticoagulation for at least 3 months
- continuing anticoagulation after this period is partly determined by whether the VTE was provoked or unprovoked
 - a provoked VTE is due to an obvious precipitating event e.g. immobilisation following major surgery. The implication is that this event was transient and the patient is no longer at increased risk
 - an unprovoked VTE occurs in the absence of an obvious precipitating event, i.e. there is a possibility that there are unknown factors (e.g. mild thrombophilia) making the patient more at risk from further clots
- if the VTE was provoked the treatment is typically stopped after the initial 3 months (3 to 6 months for people with active cancer)
- if the VTE was unprovoked then treatment is typically continued for up to 3 further months (i.e. 6 months in total)
 - NICE recommend that whether a patient has a total of 3-6 months anticoagulant is based upon balancing a person's risk of VTE recurrence and their risk of bleeding
 - the ORBIT score can be used to help assess the risk of bleeding
 - NICE state: '*Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks.*'. The implication of this is that in the absence of a bleeding risk factors, patients are generally better off continuing anticoagulation for a total of 6 months



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Textbooks

High-yield textbook

Extended textbook

Links

NICE

👍 5 🗑 0

[2020 Venous thromboembolism guidelines](#)

[Suggest link](#)

[Report broken link](#)

Media



[Deep vein thrombosis](#)

Osmosis - YouTube

👍 3 🗑 0



[Understanding Deep Vein Thrombosis \(DVT\)](#)

Zero To Finals - YouTube

👍 2 🗑 1



[Deep Vein Thrombosis - Overview \(pathophysiology, treatment, complications\)](#)

Armando Hasudungan - YouTube

👍 3 🗑 2

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Score: **20.2%**

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